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_____

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Searcher: JOHN DANTZMAN	NA Sequence (#)_____		STN	✓
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Date Completed: 5-26-00	Litigation	_____	Lexis/Nexis	_____
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Online Time: 68	Other	_____	Other (specify)	_____

PTO-1590 (1-2000)

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     (FILE 'HOME' ENTERED AT 11:54:08 ON 26 MAY 2000)

     FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, LIFESCI, WPIDS,
     JICST-EPLUS, PHIN, PHIC, BIOTECHDS, BIOBUSINESS, PROMT, CONFSCI, DRUGB'
     ENTERED AT 11:54:51 ON 26 MAY 2000
L1          157 S CINCOTTA L?/AU
L2          402 S CINCOTTA A?/AU
L3           37 S L1 AND L2
L4          522 S L1-L3
L5       186061 S PROLACTIN?
L6            3 S L3 AND L5
L7          146 S L4 AND L5
L8           37 S L3 OR L6
L9           16 DUP REMOV L8 (21 DUPLICATES REMOVED)
L10       20729 S L5 AND (TUMOR? OR TUMOUR)
L11         472 S L5 AND (ANTITUMOR OR ANTITUMOUR?)
L12       13112 S L5 AND (NEOPLAS? OR ANTINEOPLAS?)
L13        6513 S L5 AND (CANCER OR ANTICANCER?)
L14       28592 S L10-L13
L15           5 S L14 AND (PHOTOSENS? OR PHOTOACTIV? OR PHOTO ACTIV?)
L16           0 S L14 AND (PHOTO(5A)SENSIT?)
L17           0 S L14 AND ?BENZOPHENOXAZINE?
L18         739 S L14 AND (LIGHT OR PHOTO? OR UV OR ULTRAVIOLET? )
L19         928 S L14 AND (RADIAT? OR IR OR INFRARED? OR LASER?)
L20           0 S L14 AND BENZO(4W)PHENOTHIAZINIUM
L21        1625 S L18 OR L19
L22        1439 S L21 AND PROLACTIN
L23         782 DUP REMOV L22 (657 DUPLICATES REMOVED)
L24       10275 S L5(10A)(TUMOR? OR TUMOUR OR ANTITUMOR OR ANTITUMOUR? OR NEO
L25        4360 S L5(10A)(NEOPLAS? OR ANTINEOPLAS? OR CANCER OR ANTICANCER?)
L26       11719 S L24 OR L25
L27      435757 S (LIGHT OR PHOTO? OR UV OR ULTRAVIOLET? OR RADIAT? OR IR OR
IN
L28       55613 S (LIGHT OR PHOTO? OR UV OR ULTRAVIOLET? OR RADIAT? OR IR OR
I
L29         333 S L26 AND (L27 OR L28)
L30         153 DUP REMOV L29 (180 DUPLICATES REMOVED)
L31         142 S L26(15A)(L27 OR L28)
L32          64 DUP REMOV L31 (78 DUPLICATES REMOVED)
L33          76 S L29 AND (PHOTODYNAMIC? OR ENDOCRINE?)
L34         101 S L31 NOT L33
L35          56 DUP REMOV L33 (20 DUPLICATES REMOVED)
L36           6 S L34 AND PHOTO?
L37           2 S L29 AND PHOTOSEN?
L38           0 S L29 AND PHOTO SENSITI?
L39          34 S L29 AND PHOTO?
L40         105 S L33 OR L36-L39
L41          66 DUP REMOV L40 (39 DUPLICATES REMOVED)
L42           2 S L5 AND (BENZOPHENOTHIAZ? OR BENZO(2W)PHENOTHIAZ?)
L43          23 S L5 AND (ETNBS OR BPD)
L44          24 S L42 OR L43
L45           2 S L44 AND (PHOTO? OR RADIAT? OR IRRAD?)
L46           0 S L43 AND PHOTOSENSI?
L47         156 S L5 AND PHOTOSENSI?
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Searched by John Dantzman 703-308-4488

L48	179	S	L44 OR L47
L49	157	S	L48 AND (PHOTO? OR RADIAT? OR IRRAD?)
L50	5	S	L49 AND (TUMOR? OR TUMOUR)
L51	2	S	L49 AND (ANTITUMOR OR ANTITUMOUR?)
L52	2	S	L49 AND (NEOPLAS? OR ANTINEOPLAS?)
L53	1	S	L49 AND (SARCOM? OR ANTISARCOM?)
L54	5	S	L50-L53

=> D BIB ABS

L41 ANSWER 1 OF 66 MEDLINE DUPLICATE 1
AN 1999300316 MEDLINE
DN 99300316
TI Timed daily administration of **prolactin** and corticosteroid hormone reduces murine **tumor** growth and enhances immune reactivity.
AU Keisari Y; Cincotta E; Meier A H; Cincotta A H
CS Ergo Science Corporation, Charlestown, Massachusetts 02129, USA.
SO CHRONOBIOLOGY INTERNATIONAL, (1999 May) 16 (3) 315-33.
Journal code: CYT. ISSN: 0742-0528.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199909
EW 19990905
AB In the present study, we investigated the time-dependent interactive effects of daily injections of prolactin (PRL) and corticosterone (CORT) on the activation of lymphocyte function and inhibition of tumor growth in vivo in mice. BALB/c mice were injected subcutaneously with EMT-6 fibrosarcoma cells (a murine connective tissue tumor cell derived from mammary gland), and then different groups of animals were treated with PRL (1 microg/g body weight [BW] ip) at Oh, 4h, 8h, 12h, 16h, or 20h after CRT (1 microg/g BW ip) daily for 10 days. Different control groups were vehicle treated or treated with either hormone alone. Mice were kept in constant light 1 week before and during injections and in a 14:10 **light**-dark cycle thereafter. **Tumor** progression was monitored for up to 21 days after the cessation of treatment, and thereafter spleen lymphocytes were harvested and tested for mitogen-triggered proliferation. **Prolactin** administration at 8h or 16-20h after corticosteroid treatment reduced **tumor** volume by 77% and 49%, respectively, relative to vehicle-treated controls. Other time relations of hormone treatment were ineffectual. Further studies indicated that the immunosuppressant cyclosporin A (CSA) substantially stimulated tumor growth; this effect was completely abrogated by a simultaneous 8h related hormone treatment. How ever, the 8h hormone treatment was ineffective in inhibiting tumor growth in T-cell-deficient nude mice. Spleen lymphocytes from tumor-bearing (TB) mice showed an elevated basal proliferative capacity stimulated by concanavalin A (ConA; a stimulus for T-cell proliferation) and lipopolysaccharide (LPS; a stimulus for B-cell proliferation) compared to non-TB mice. Spleen lymphocytes from TB mice treated with CORT and PRL at 8h intervals exhibited an increased spontaneous (as well as LPS- and ConA- triggered) proliferation (by 104%, 48%, and 70%, respectively) compared with vehicle control TB mice. Fluorescence-activated cell sorting (FACS) analysis of splenocytes from hormone-treated animals indicated a 34-100% increase in the CD4+ (e.g., T helper cell) population. Treatment of animals with either hormone alone did not inhibit tumor growth or stimulate immune function relative to vehicle controls. The daily rhythms of plasma PRL, CORT, and thyroxine were all substantially altered by the presence of

tumor in these mice. These results indicate that appropriately timed daily
treatment of PRL and CORT can attenuate tumor growth, in part, via activation of antitumor immune mechanisms. Collectively, these data suggest that circadian neuroendocrine activities must be temporally organized appropriately to inhibit tumor growth.

=> D BIB ABS 2

L41 ANSWER 2 OF 66 MEDLINE DUPLICATE 2
AN 1999103662 MEDLINE
DN 99103662
TI Differential expression of **prolactin** receptor (PRLR) in normal and **tumorous** adrenal tissues: separation of cellular **endocrine** compartments by **laser** capture microdissection (LCM).
AU Glasow A; Haidan A; Gillespie J; Kelly P A; Chrousos G P; Bornstein S R
CS Department of Internal Medicine III, University of Leipzig, Germany.
SO ENDOCRINE RESEARCH, (1998 Aug-Nov) 24 (3-4) 857-62.
Journal code: EIH. ISSN: 0743-5800.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199906
EW 19990603
AB PRL stimulates adrenal steroidogenesis. In this study, we compared the PRLR expression in normal and tumorous adrenal tissues and investigated a potential proliferative effect of PRL in adrenal cells. mRNA expression of long and intermediate forms of PRLR was detected in both normal adrenal cortex as well as benign and malignant adrenal tumors and in the human adrenocortical carcinoma cell line NCI-H295. Molecular analysis of cells procured by LCM clearly demonstrated that PRLR mRNA is expressed in the adrenal cortex but not in the medulla. Immunostaining revealed PRLR protein in all three zones of the normal adrenal cortex. Furthermore, adrenal carcinomas and adenomas stained positive for the PRLR, while in phaeochromocytomas as in the normal adrenal medulla, no specific staining was observed. By WST-1 test, we could show that PRL (10(-7) M) decreased proliferation and viability of adrenal cells in primary cell culture suggesting that PRL is not a mitogenic factor of adrenocortical cells.

=> D BIB ABS 4

L41 ANSWER 4 OF 66 MEDLINE DUPLICATE 5
AN 94249117 MEDLINE
DN 94249117
TI Aggressive small cell tumor of the skull base.
AU Arnesen M; Scheithauer B W
CS Department of Pathology, Abbott Northwestern Hospital, Minneapolis, Minnesota 55407..
SO ULTRASTRUCTURAL PATHOLOGY, (1994 Jan-Apr) 18 (1-2) 191-7.
Journal code: WMM. ISSN: 0191-3123.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199408
AB A 40-year-old Black man presenting with increasing nasal discharge of bloody, mucoid pus as well as nasal obstruction over a 2-month period is described. Magnetic resonance imaging of the skull showed a tumor eroding through the skull base into the clivus and extending into the sphenoid sinus. Endoscopy of the sphenoid sinus demonstrated a polypoid mass extending into the posterior choanae. The lesion was partially resected. Histologic evaluation showed a cellular small blue cell tumor punctuated by bland, epithelial-lined microcysts. Electron microscopy revealed epithelial cells with abundant rough endoplasmic reticulum and electron-dense membrane-bound **endocrine** granules, some undergoing misplaced exocytosis. Immunohistochemical evaluation demonstrated cytoplasmic reactivity for neuron-specific enolase, synaptophysin, and prolactin. Stains for leukocyte common antigen, HMB-45, desmin, cytokeratin, chromogranin, and the remaining spectrum of pituitary hormones including growth hormone, corticotropin, luteinizing hormone, follicle-stimulating hormone, and thyrotrophic hormone were negative. In contrast, the epithelium lining the cysts was cytokeratin positive and synaptophysin negative. This ostensibly small cell **tumor** therefore represented a remarkably extensive and aggressive **prolactin cell** adenoma with unusual **light** microscopic features. Characterization of the lesion required electron microscopy and further confirmation by immunocytology. The distinction of pituitary adenomas and particularly of **prolactin** cell **tumors** from other adenoma types and from other small cell lesions markedly affects therapy and patient prognosis.

=> D BIB ABS 5

L41 ANSWER 5 OF 66 MEDLINE DUPLICATE 6
AN 93321413 MEDLINE
DN 93321413
TI Intracranial dissemination of a macroprolactinoma.
AU Assies J; Verhoeff N P; Bosch D A; Hofland L J
CS Department of Psychiatry, Academic Medical Centre, Amsterdam, The Netherlands..
SO CLINICAL ENDOCRINOLOGY, (1993 May) 38 (5) 539-46.
Journal code: DCI. ISSN: 0300-0664.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199310
AB A patient with a macroprolactinoma and extrasellar extension was treated by incomplete transfrontal surgery, external irradiation and additional bromocriptine (Br) treatment. After 4 years, partial bromocriptine resistance developed (a rare occurrence) together with the appearance of intracranial metastases. 123I-Iodobenzamide was helpful in evaluating the dopamine D2 receptor status of the metastatic **tumour** both in vivo using single-**photon** emission computed tomography (SPECT) and in vitro. **Prolactin** release by the cultured metastatic **tumour** cells was more potently inhibited by CV 205-502 than by bromocriptine. The patient, treated by surgery, irradiation and CV 205-502, developed a ptosis of the left eye and a transient psychiatric delusional state, the latter probably an effect of the dopamine agonist. As the right frontal metastasis was markedly positive on SPECT with 111In-SMS, somatostatin treatment was added to the CV 205-502.

=> D BIB ABS 6-20

L41 ANSWER 6 OF 66 MEDLINE DUPLICATE 7
AN 93135924 MEDLINE
DN 93135924
TI Serum immunoreactive and bioactive lactogenic hormones in advanced breast cancer patients treated with bromocriptine and octreotide.
AU Anderson E; Ferguson J E; Morten H; Shalet S M; Robinson E L; Howell A
CS Department of Clinical Research, Christie Hospital NHS Trust, Manchester, U.K..
SO EUROPEAN JOURNAL OF CANCER, (1993) 29A (2) 209-17.
Journal code: ARV. ISSN: 0959-8049.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199304
AB 6 patients with advanced breast cancer who had failed first and second line **endocrine** therapies received bromocriptine (1.25-2.5 mg twice daily per os) and octreotide (Sandostatin) via a continuous subcutaneous infusion (200-400 micrograms/24 h) until disease progression.
Pre-treatment 24-h profiles of serum lactogenic hormones and their response to standard provocative tests were established and repeated at 2 weeks, and 3 and 6 months (or at **tumour** progression). Immunoreactive **prolactin** (**ir**-PRL), growth hormone (**ir**-GH) and insulin-like growth factor I (IGF-I) were measured by radioimmunoassay and bioactive lactogenic hormone levels (BLH) were estimated using the Nb2 rat lymphoma **cell** bioassay. Before treatment all patients showed episodic secretion of **ir**-PRL, ir-GH and BLH and provocative stimuli resulted in a peak of ir-GH and BLH maximal between 60 and 90 min after injection but no change in ir-PRL. After 2 weeks of treatment, ir-PRL levels were reduced to below the limit of detection in all 6 patients. Peaks of ir-GH and BLH were still apparent, although much reduced. Immunoreactive PRL continued to be profoundly suppressed in 3 of the 4 patients who remained on treatment for 3 to 6 months. Small pulses of ir-GH were still detectable in these patients with which BLH was, again, well correlated. After 2 weeks of treatment, serum IGF-I levels were reduced by 9-54% of the pretreatment values and generally remained suppressed throughout treatment. Clinically, 4 patients did not show disease progression for periods of up to 6 months and side-effects were minimal.

L41 ANSWER 7 OF 66 MEDLINE DUPLICATE 8
AN 90323099 MEDLINE
DN 90323099
TI Regulation and molecular characterization of dopamine D2 receptors in a **prolactin**-secreting 7315a anterior pituitary **tumor**.
AU Lew J Y; Zawadzka H; Feigenblum D; Tang D; Filer D; Benedetto P; Goldstein M
CS Department of Psychiatry, New York University Medical Center, NY 10016.
NC MH 43230 (NIMH)

MH 02717 (NIMH)
06801
SO EUROPEAN JOURNAL OF PHARMACOLOGY, (1990 Jun 12) 188 (6) 329-34.
Journal code: EN6. ISSN: 0014-2999.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199011
AB The regulation and molecular properties of the dopamine (DA) D2 receptors were compared in the **prolactin**-secreting 7315a anterior pituitary **tumor** with those in the striatum of rats. Chronic treatment with haloperidol increases the maximal binding for [3H]spiroperidol in tumor and striatum, but the percent increase is much higher in **tumor** than in striatum. **Photoaffinity** labelling of DA D2 receptors with N-(p-azido-m-[125I]iodophenethyl)spiperone ([125I]N3-NAPS) yielded a major specifically labeled peptide with the Mr of 32-34 kDa in tumor, and two specifically labeled peptides with Mr of 32-34 and 92-94 kDa in striatum. The analysis of DA D2 receptor mRNA shows that the size is similar in tumor and striatum. The DA D2 receptor mRNA in tumor is very low and chronic treatment with haloperidol produces a considerable increase of the specific mRNA. It is postulated that the reported defect in regulation of prolactin release by DA agonists might be due to posttranslational changes in the tumor DA D2 receptor.

L41 ANSWER 8 OF 66 MEDLINE DUPLICATE 9
AN 89087477 MEDLINE
DN 89087477
TI A 64 kDa protein is a candidate for a thyrotropin-releasing hormone receptor in **prolactin**-producing rat pituitary **tumor** cells (GH4C1 cells).
AU Wright M; Hogset A; Alestrom P; Gautvik K M
CS Institute of Medical Biochemistry, University of Oslo, Norway.
SO BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1988 Dec 30) 157 (3) 875-82.
Journal code: 9Y8. ISSN: 0006-291X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198904
AB A thyrotropin-releasing hormone (TRH) binding protein of 64 kDa has been identified by covalently crosslinking [3H]TRH to GH4C1 **cells** by **ultraviolet** illumination. The crosslinkage of [3H]TRH is **UV**-dose dependent and is inhibited by an excess of unlabeled TRH. A 64 kDa protein is also detected on immunoblots using an antiserum raised against GH4C1 cell surface epitopes. In a closely related cell line (GH12C1) which does not bind [3H]TRH, the 64 kDa protein cannot be demonstrated by [3H]TRH crosslinking nor by immunoblotting. These findings indicate that the 64 kDa protein is a candidate for a TRH-receptor protein

=> D BIB ABS 3

L41 ANSWER 3 OF 66 MEDLINE DUPLICATE 4
AN 95290703 MEDLINE
DN 95290703
TI **Photoperiodic** effects on **tumor** development and immune function.
AU Nelson R J; Blom J M
CS Department of Psychology, Johns Hopkins University, Baltimore, Maryland 21218, USA..
NC HD 22201 (NICHD)
CA 58168 (NCI)
P30 HD 06268 (NICHD)
SO JOURNAL OF BIOLOGICAL RHYTHMS, (1994 Winter) 9 (3-4) 233-49.
Journal code: A9L. ISSN: 0748-7304.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199509
AB Seasonal changes in adaptations associated with winter coping strategies have been frequently studied. Central among the suite of energy-saving, winter-coping strategies is the suspension of reproductive activities. The inhibition of reproduction by nontropical rodents is mediated by daylength changes. Although balanced annual energy budgets are critical, survival and subsequent reproductive success also require avoiding predators, illness, and early death. Because the stressors of winter could lead to suppressed immune function, we hypothesized that animals should have evolved survival strategies involving immunoenhancement. Short daylengths provide a predictive cue to individuals that could be used to enhance immune function in advance of stress-induced immunosuppression. In Experiment 1, adult female deer mice (Peromyscus maniculatus) were housed in either long (LD 16:8) or short (LD 8:16) days for 8 weeks, then injected with the chemical carcinogen 9,10-dimethyl-1,2-benzanthracene (DMBA) dissolved in dimethyl sulfoxide (DMSO) or with the DMSO vehicle alone. Animals were evaluated weekly for 8 weeks after injection. None of the animals treated with DMSO developed tumors in any of the experiments. Nearly 90% of the long-day deer mice injected with DMBA developed squamous cell carcinoma. None of the short-day deer mice injected with DMBA developed tumors. Small lesions developed at the site of injection; short-day females had less severe lesions and healed faster than long-day females. Immunoglobulin G (IgG) response to i.p. injection of sheep red blood **cells** (SRBC) did not differ **photoperiodic** conditions. The role of estrogens in the **photoperiodic** responses was evaluated in Experiment 2: Ovariectomized or sham-ovariectomized deer mice received estradiol benzoate replacement therapy or a control procedure in long daylengths for 8 weeks prior to injection of DMBA or DMSO, then were monitored for 8 additional weeks. Females treated with DMBA developed tumors at the same rate, regardless of estrogen manipulation. Estrogen did not affect healing rates. In Experiment 3, female deer mice were injected with a slurry of microspheres that either contained bromocriptine or were empty. Suppression of **prolactin**

with bromocriptine resulted in a decrease of **tumor** incidence from 55.6% to 24% in long-day females 8 weeks after injection with DMBA. Healing rates were not affected by prolactin manipulations. Silastic capsules that were filled with either melatonin or cholesterol were implanted into long-day female deer mice in Experiment 4; 8 weeks later, females received an injection of either DMBA or DMSO, then were monitored for 8 weeks.(ABSTRACT TRUNCATED AT 400 WORDS)

in GH4C1 cells.

L41 ANSWER 9 OF 66 MEDLINE DUPLICATE 10
AN 89153326 MEDLINE
DN 89153326
TI Necroses of prolactin-secreting pituitary adenomas under treatment with dopamine agonists: light microscopical and morphometric studies.
AU Hallenga B; Saeger W; Ludecke D K
CS Department of Pathology, Marienkrankenhaus Hamburg, FRG.
SO EXPERIMENTAL AND CLINICAL ENDOCRINOLOGY, (1988 Sep) 92 (1) 59-68.
Journal code: EPA. ISSN: 0232-7384.
CY GERMANY, EAST: German Democratic Republic
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198906
AB In order to clarify the mechanism by which prolactin-secreting adenomas reduce in size during treatment with dopamine agonists (DA), we studied altogether 18 chromophobe pituitary adenomas by carrying out **light** microscopical **cell** counting of necrobiotic alterations and necroses in **photographs** of semi-thin sections. Depending on hormonal activity and preoperative treatment of the patients 3 groups of adenomas were formed: 6 prolactin producing adenomas were treated with bromocriptine and lisuride (group 3). 8 cases remained preoperatively without medical treatment (group 2). For comparison, we studied 4 cases of clinically inactive pituitary adenomas (group 1). All adenomas were immunohistologically positive for **prolactin**. By classifying each **tumor** cell in one of four stages of necrotic alteration (stage 1: intact cell, stage 2: slightly condensed nucleus and shrunken cytoplasm, stage 3: necrotic cell with still visible nuclear membrane, stage 4: cell debris) we arrived at an index for necrobiotic alterations of the 18 adenomas. We found a significantly higher rate of cell necroses in DA-treated **tumors** compared with preoperatively untreated **prolactinomas** and inactive adenomas. Previous investigations in this field have revealed that a reduction in cell size may well cause the shrinkage of the prolactinomas after DA-therapy. The results presented in this paper indicate, however, that the role of necroses now needs to be given much closer attention as an additional factor.

L41 ANSWER 10 OF 66 MEDLINE DUPLICATE 11
AN 88061494 MEDLINE
DN 88061494
TI Hyperprolactinemia and hypothyroidism following cytotoxic therapy for central nervous system malignancies.
AU Constine L S; Rubin P; Woolf P D; Doane K; Lush C M
CS Department of Radiation Oncology, University of Rochester Medical Center, NY 14642..
SO JOURNAL OF CLINICAL ONCOLOGY, (1987 Nov) 5 (11) 1841-51.
Journal code: JCO. ISSN: 0732-183X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198803
AB Endocrinologic dysfunction including hyperprolactinemia and hypothyroidism

are recognized complications of irradiation to the hypothalamic-pituitary axis or thyroid gland in the course of treating CNS malignancies. However, the frequency of these adverse effects in both short- and long-term survivors may be underestimated. Sixty-five patients treated in the University of Rochester **Cancer** Center since 1968 with **radiation** with or without BCNU chemotherapy for CNS **tumors** not involving the hypothalamic-pituitary axis were evaluated for thyroid, **prolactin**, and gonadal disturbances regardless of clinical symptomatology. Prolactin values were elevated in 19 of 47 patients (40%). For males and females treated with greater than 55 Gy, abnormal values were present in nine of 11 (82%) and seven of 14 (50%), respectively. For males and females treated with less than or equal to 55 Gy, two of nine (22%) and one of 13 (8%), respectively, were abnormal (P = .0001). Six of six patients who also received BCNU chemotherapy were hyperprolactinemic, as compared with six of ten (60%) who did not receive BCNU. Seven of eight females with elevated prolactin levels had menstruation abnormalities, and five of seven adult males noted a decrease in libido. Mild abnormalities in testosterone concentration were found in three of nine men evaluated, all of whom had normal gonadotropins. Of 47 patients who did not receive irradiation to the spinal axis (and thus the thyroid gland), ten (21%) had a decreased thyroxin (T4) value. Only one of these patients had an elevated thyroid-stimulating hormone (TSH) value. Of 32 patients who received greater than 55 Gy, ten (31%) had a low T4, compared with zero of 15 who received less than or equal to 55 Gy (P = .0001). Four of eight patients (50%) who also received BCNU had low T4 values, as compared with three of 14 (21%) who did not receive BCNU. Of 15 patients who were treated with 4 to 10 MV **photon** irradiation to the spinal axis, five patients (33%) had elevated TSH values. The mean spinal axis dose in these patients was 33 Gy. Two euthyroid children in this group manifested the early onset of puberty. The complex of endocrinologic abnormalities observed in several patients receiving only cranial irradiation, that is elevated prolactin, decreased thyroid, and gonadal hormone secretion in the presence of otherwise normal pituitary hormone levels, suggests a radiation-induced insult to the hypothalamic regulation of pituitary function.

L41 ANSWER 11 OF 66 MEDLINE DUPLICATE 12
AN 85287168 MEDLINE
DN 85287168
TI Pathobiologic study of pituitary tumors: report of 62 cases with a review of the recent literature.
AU Challa V R; Marshall R B; Hopkins M B 3d; Kelly D L Jr; Civantos F
SO HUMAN PATHOLOGY, (1985 Sep) 16 (9) 873-84.
Journal code: GEC. ISSN: 0046-8177.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 198512
AB Advances in radioimmunoassay procedures, immunocytochemistry, neuroradiologic imaging, and the surgical and medical treatment of

pituitary adenomas have led to reappraisal of their classification as well as refinements in the diagnostic approaches used by pathologists. Sixty-two pituitary adenomas are described, and recent advances in this field are reviewed. Most of the patients were adults, but one of the adrenocorticotropic hormone (ACTH)-producing adenomas occurred in an 11-month-old infant. **Endocrine**-inactive tumors (43.5 per cent) were less common than hormone-producing tumors (56.5 per cent). Local invasion was most common in the former group, followed by ACTH-producing and other hormone-producing tumors. Ultrastructural features correlated with hormonal levels in the growth hormone(GH)-secreting **tumors** but not in the **prolactin**(LTH)- or ACTH-producing **tumors**. The formation of 7-nm filaments in the cytoplasm of **tumor cells**, corresponding to Crooke's hyaline change on **light** microscopy, was characteristic of ACTH-producing **tumors**. Ultrastructural changes in the ACTH granules suggested that the filaments may be derived from the feedback action of cortisol. Prior to surgery, a Rathke's cleft cyst and a chordoma were mistaken for **endocrine**-inactive pituitary adenomas. In two additional cases ectopic ACTH-producing tumors of lung clinically mimicked pituitary adenoma. Conversely, one pituitary adenoma mimicked sphenoid wing meningioma. Clinical, hormonal, and radiologic data and immunocytochemical and electron microscopic studies are needed for accurate pathologic interpretation and classification of pituitary adenomas.

L41 ANSWER 12 OF 66 MEDLINE DUPLICATE 13
AN 86177147 MEDLINE
DN 86177147
TI In-vitro effects of bromocriptine on isolated pituitary adenoma cells. Ultrastructural and morphometrical studies.
AU Saeger W; Thiel M; Caselitz J; Ludecke D K
SO PATHOLOGY, RESEARCH AND PRACTICE, (1985 Dec) 180 (6) 697-704. Journal code: PBZ. ISSN: 0344-0338.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 198607
AB 3 pituitary adenomas in hyperprolactinemia and 3 GH and **prolactin** producing **tumours** were analysed. The adenoma cells were prepared and held in suspension so that they could be treated with bromocriptine (10 ng and 100 ng). At different times after treatment (0.5, 60 and 90 minutes), the **cells** were fixed and prepared for conventional electronmicroscopy. Electron microscopic **photographs** were quantitatively analysed by the point counting method. The results were compared to those of an untreated control group. After bromocriptine influence, there was a decrease of the hormone secretion into the supernatant (2 of 3 prolactin producing adenomas). The prolactin secretion was unchanged in all 3 adenomas which produced prolactin and GH, but there was a decrease in the GH production in 1 of these cases. Ultrastructural morphometry revealed the following results: In prolactin producing adenomas, there was a decrease in the number of exocytoses, an increase in the volume density of lysosomes (2 cases) and an increase of the rough endoplasmic reticulum (1 case). The decrease of the "unorganized"

cytoplasm was observed in all 3 cases, but was significant only in 1 case.
There was a significant increase in secretory granules (1 case). In adenomas which produced prolactin and GH displayed a significant increase of the rough endoplasmic reticulum and of the granules. The outlines of the cellular membranes seemed smoother (1 case). The heterogeneous results
may be interpreted as an expression of the reduced hormone secretion (secretory granules, lysosomes), some data are in accordance with the beginning of necrobiotic phenomena (rough endoplasmic reticulum). The decrease of the "unorganized" cytoplasm may be due to a shrinking process.

L41 ANSWER 13 OF 66 MEDLINE DUPLICATE 14
AN 83293514 MEDLINE
DN 83293514
TI Transsphenoidal microsurgery of pituitary macroadenomas with long-term follow-up results.
AU Ciric I; Mikhael M; Stafford T; Lawson L; Garces R
SO JOURNAL OF NEUROSURGERY, (1983 Sep) 59 (3) 395-401.
Journal code: JD3. ISSN: 0022-3085.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals; Cancer Journals
EM 198312
AB The authors have reported on 108 patients with pituitary macroadenomas (measuring 2 cm in at least one diameter) who underwent 117 transsphenoidal operations and five craniotomies, and were followed for periods ranging from 6 months to 14 years. Vision improved in 90% of the patients. Gross total tumor removal with no evidence of residual tumor tissue demonstrable on the postoperative computerized tomography scan was accomplished in 41% of cases. However, gross total tumor removal is not synonymous with complete **tumor** removal. **Endocrine** cure was possible in 25% of **prolactin**-secreting and 20% of growth hormone-secreting adenomas. The incidence of recurrence was 12%, with the majority occurring from 4 to 8 years postoperatively. Both the tumors with suprasellar extension of more than 2 cm and the hard fibrotic **tumors** had a higher recurrence rate. Postoperative administration of **radiation** therapy has been associated with a significantly lower recurrence rate than when this therapy was withheld. Transsphenoidal
surgery of pituitary macroadenomas confined to the extra-arachnoid space is associated with a relatively small number of complications. The operative technique used in this series is described.

L41 ANSWER 14 OF 66 MEDLINE DUPLICATE 15
AN 81083274 MEDLINE
DN 81083274
TI Diurnal variation of **prolactin** secretion differentiates pituitary **tumors** from the primary empty sella syndrome.
AU Malarkey W B; Goodenow T J; Lanese R R
NC RR-34 (NCRR)
SO AMERICAN JOURNAL OF MEDICINE, (1980 Dec) 69 (6) 886-90.
Journal code: 3JU. ISSN: 0002-9343.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Abridged Index Medicus Journals; Priority Journals
EM 198104
AB In an attempt to find an **endocrine** function test that might be useful in differentiating the primary empty sella syndrome from a pituitary **tumor**, we evaluated 24-hour **prolactin** levels in seven patients with the primary empty sella syndrome, 16 patients with pituitary tumors and 37 normal subjects. All eight patients with the primary empty sella syndrome had normal 24-hour mean prolactin levels and normal diurnal variation of **prolactin** release whereas in each patient with a pituitary **tumor** nocturnal **prolactin** secretion was blunted. In **light** of these findings and those of other investigators, we do not perform routine invasive study of the pituitary in patients with (1) a typical clinical presentation of the empty sella syndrome, (2) no endocrinopathies, (3) a normal computerized axial tomography scan, when indicated, and (4) normal serum prolactin levels with intact diurnal variation.

L41 ANSWER 15 OF 66 MEDLINE DUPLICATE 18
AN 77180226 MEDLINE
DN 77180226
TI [**Endocrine** polyadenomatosis associated with prolactin pituitary adenoma and an intrathyroidal parathyroid adenoma].
Polyadenomatose endocrinienne associant un adenome hypophysaire `a prolactine et un adenome parathyroidien intrathyroidien.
AU Tourniaire J; Trouillas J; Maillet P; David L; Pallo D; Tran Minh V; Bressot C
SO ANNALES D ENDOCRINOLOGIE, (1977) 38 (1) 1-11.
Journal code: 540. ISSN: 0003-4266.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
LA French
FS Priority Journals
EM 197708
AB A pituitary adenoma was removed transsphenoidally from a 20-yr-old woman with secondary amenorrhea, galactorrhea, and hyperprolactinemia. **Light** and electronic microscopy, immunocytology characterized a **prolactin cell tumor.** The patient also underwent three surgical explorations for hyperparathyroidism. Only after selective catheterization of thyroid veins with radioimmunoassay for parathormone, an intrathyroidal parathyroid adenoma was found. No other case of proven prolactin adenoma in Wermer's syndrome has been reported.

L41 ANSWER 16 OF 66 MEDLINE DUPLICATE 19
AN 76056685 MEDLINE
DN 76056685
TI [Pituitary adenomas of patients with galactorrhea. Light and electron microscopic studies (author's transl)].
Hypophysenadenome bei Galactorrhoe. Licht- und elektronenoptische Untersuchungen.
AU Saeger W
SO VIRCHOWS ARCHIV. A, PATHOLOGICAL ANATOMY AND HISTOLOGY, (1975 Oct 20) 368 (2) 123-39.
Journal code: XD0.
CY GERMANY, WEST: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
LA German

FS Priority Journals
EM 197603
AB A collection of 108 surgically removed pituitary adenomas was studied by histologic, immunohistochemical and electron microscopical methods. It included 7 predominantly chromophobe adenomas of patients whose clinical symptoms consisted of a pure galactorrhea. Ultrastructurally, 4 of these adenomas contained little endoplasmic reticulum so that an **endocrine** activity of the tumors could not be assumed. These cases represented inactive adenomas which probably led to a disturbance of the secretion of prolactin-inhibiting factor by suprasellar extension resulting in stimulation of the non-tumorous adenohypophysis and secondary hyperprolactinemia. Another 3 adenomas consisted of cells that showed histologic and immunocytochemical reactions of the same kind as normal prolactin cells. Electron microscopically, these adenoma cells exhibited a very well developed rough-surfaced endoplasmic reticulum, dilatation of the Golgi complexes, sparsely arranged pleomorphic secretory granules, an increased number of microtubules, and interdigitating microvilli formed by the cell membrane. These features resembled closely the characteristics of stimulated non-**tumorous prolactin** cells during lactation, and thus could be termed "**prolactin** cell adenomas". These **tumors** surely caused a hyperprolactinemia through their own hormone production. In addition 3 other adenomas were present which showed the same **light** and electron microscopic structures as the prolactin **cell** adenomas but did not cause galactorrhea. From the findings in these cases we assume that the tumors effected neither a clinically peculiar hyperprolactinemia nor produced an endocrinologically inactive polypeptide.

L41 ANSWER 17 OF 66 MEDLINE
AN 92263228 MEDLINE
DN 92263228
TI [Hypophyseal dysfunction and tumors].
Hypophysendysfunktion und-tumoren.
AU Burgi U; Seiler R
CS Abteilung fur Endokrinologie und Diabetologie, Inselspital, Bern..
SO THERAPEUTISCHE UMSCHAU, (1992 Mar) 49 (3) 136-41. Ref: 11
Journal code: VPT. ISSN: 0040-5930.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA German
EM 199208
AB Some pituitary hormones secrete hormones while others do not. Nonsecreting tumors can interfere with normal pituitary hormone secretion and produce tumor symptoms and signs like headaches and visual field defects. The most frequent hormone-secreting **tumors** are **prolactinomas**. Growth hormone or ACTH or gonadotropin or gonadotropin-alpha and beta chain-producing tumors are less frequent, TSH producing tumors are extremely rare. The most important elements of the diagnostic work-up are clinical signs and symptoms, assessment of pituitary function (measurement

of TSH, free T4, LH, FSH, oestradiol/free testosteron, growth hormone, IGF-1, prolactin, ACTH, Cortisol, serum and urine osmolality), CT and/or MRI and, in patients with large tumors, a visual field exam. The treatment of choice of pituitary **tumors** is often surgery. Alternative therapies are **radiation** treatment (in nonoperable patients or when hormone levels are persistently elevated after pituitary surgery) and drug treatment (dopamine agonists in hyperprolactinemia, somatostatin analogues in acromegaly). Pituitary hormone deficiencies are treated depending on the specific deficiency with thyroxine, cortisone, oestrogen/gestagen/testosterone gonadotropines or ADH analogues.

L41 ANSWER 18 OF 66 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 3
AN 1997:740112 HCAPLUS
DN 128:11512
TI Growth inhibition and eradication of **tumors** using neuroendocrine resetting therapy and **photodynamic** therapy
IN Cincotta, Anthony H.; Cincotta, Louis
PA Ergo Science Incorporated, USA; General Hospital Corporation; Rowland Institute for Science
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9740829	A1	19971106	WO 1997-US7577	19970415
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 910365	A1	19990428	EP 1997-922668	19970415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-16619 19960501
WO 1997-US7577 19970415
AB A method of ablating the growth of or eradicating **tumors** in mammals having **prolactin**, growth hormone, and melatonin daily rhythms involves adjusting one or more of the prolactin, growth hormone, and melatonin profiles of the mammal to conform to or approach the corresponding normal profile for healthy members of the same species and sex as said mammal, contacting the **cells** of the **tumor** with a **photoactive photosensitizer**, and, exposing the **photosensitizer**-contact **tumor cells** to **light** of a predetd. wavelength, power d., and energy level.

L41 ANSWER 19 OF 66 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 16
AN 1980:526009 HCAPLUS
DN 93:126009
TI Immunocytochemical analysis of **prolactin** production by monolayer cultures of GH3 rat anterior pituitary **tumor** cells. I. Long-term effects of stimulation with thyrotropin-releasing hormone (TRH)
AU Hoyt, Richard F., Jr.; Tashjian, Armen H., Jr.
CS Sch. Med., Boston Univ., Boston, MA, 02118, USA
SO Anat. Rec. (1980), 197(2), 153-62
CODEN: ANREAK; ISSN: 0003-276X

DT Journal
LA English
AB TRH [24305-27-9] stimulates **prolactin** [9002-62-4] prodn. in cultured GH3 rat anterior pituitary **tumor** cells. Intracellular prolactin, unaffected quant. by acetone fixation and choice of substratum, was localized immunocytochem. by a granular brown ppt. It was abolished if anti-prolactin serum was preabsorbed with rat prolactin or omitted from the protocol. Intracellular prolactin was maximized with colchicine (5.0 .times. 10-6 M; final 3 h of incubation) in control and TRH-treated (10 mg/mL; 48 h) GH3 cell cultures. A total of 8500 **cells** were classified by **light** microscopy as unstained, heavily (H) or moderately (M) stained for prolactin. In controls, 35% of cells were prolactin-pos.: 6% H and 29% M. After TRH, 45% were pos.: 7% H and 38% M. Although prolactin-pos. cells were unevenly distributed, comprising 25 - 46% of cells in individual microscopic fields in controls, TRH increased the proportion of M cells in all areas. TRH treatment raised prolactin levels to 450% of control, but math. anal. attributed < 30% of the increase to new prolactin-pos. cells. Thus, TRH acts on GH3 cultures principally by raising the mean hormone content of individual pos. cells rather than by increasing the proportion of cells committed to prolactin prodn.

L41 ANSWER 20 OF 66 HCAPLUS COPYRIGHT 2000 ACS
AN 1998:133091 HCAPLUS
DN 128:253726
TI Dynamic changes in prolactin promoter activation in individual living lactotrophic cells
AU Takasuka, N.; White, M. R. H.; Wood, C. D.; Robertson, W. R.; Davis, J. R. E.
CS Endocrine Sciences Research Group, Department of Medicine, University of Manchester, Manchester, M13 9PT, UK
SO Endocrinology (1998), 139(3), 1361-1368
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
AB The firefly luciferase gene has become widely used as a convenient reporter for studies of gene promoter regulation. Very recently, the development of ultralow-light imaging cameras has enabled the quant. digital imaging of light signals resulting from luciferase activation in the presence of luciferin substrate. The authors have applied this technol. to the study of PRL promoter activation in individual pituitary tumor cells to study the temporal and spatial characteristics of the expression of a well-characterized pituitary hormone gene. Rat pituitary GH3 cells were transfected by lipofection with a luciferase reporter gene linked to 5000 bp from the human PRL gene 5'-flanking region. A series of stably transfected cell clones were generated, and one of these was chosen for detailed study on the basis of appropriate regulation of high-level luciferase expression by a series of known stimuli including TRH, forskolin, the calcium channel agonist Bay K8644, and basic fibroblast growth factor (bFGF). These cells were subjected to direct imaging of

luciferase activity using a Hamamatsu **photon**-counting camera linked to a Zeiss Axiovert microscope with an Argus-50 image processor. Cells were exposed to 1 mM luciferin, and images were integrated over 30-min periods for up to 72 h. The total **photon** count over a given field settled to steady levels within 10 h and then remained const. for over 55 h. Addn. of forskolin, TRH, or bFGF increased the total **photon** count of fields of 20-100 **cells** by 2- to 4-fold consistent with previous data from transient expression assays using the human PRL promoter. Individual cells, showed marked temporal and spatial heterogeneity and variability of luciferase expression when studied at 3-h intervals. Unstimulated cells showed variable luciferase expression with up to 40-fold excursions in **photon** counts per single **cell** area within 12-h periods. Stimulation of cells with either TRH, forskolin, or bFGF resulted in smooth increases in **photon** output over fields of 20-100 **cells**, but again individual **cell** responses differed widely, with some **cells** showing slow progressive rises in **photon** output, others showing phasic or transient responses, and yet others showing no response. In conclusion, the authors found a surprising degree of heterogeneity and temporal variability in the level of gene expression in individual living pituitary tumor cells over long periods of time, with markedly divergent responses to hormonal or intracellular stimulation. The use of stably transfected clonal cell lines with extended periods of reporter gene imaging offers a valuable insight into control of gene expression in living cells in real time.

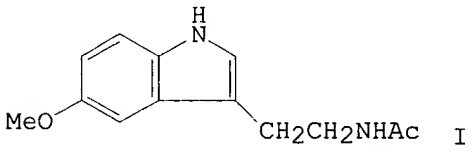
=> D BIB ABS 21-66

L41 ANSWER 21 OF 66 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:575370 HCAPLUS
DN 122:306891
TI Characterization and localization of an immunoreactive growth hormone-releasing hormone precursor form in normal and tumoral human anterior pituitaries
AU Rauch, Claudine; Li, Jacques Yuan; Croissandeau, Gilles; Berthet, Myriam; Peillon, Francoise; Pagesy, Patrick
CS Fac. Med. Pitie-Salpetriere, INSERM U-223, Paris, 75634, Fr.
SO Endocrinology (1995), 136(6), 2594-601
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
AB Arguments favor an in situ synthesis of GH-releasing hormone (GHRH) in the normal and tumoral human anterior pituitary. These tissues may express human (h) GHRH mRNA, contain hGHRH-(1-44)-NH2, and secrete in vitro an immunoreactive form (ir-form) of the peptide. Here, the authors characterize and localize the precursor of hGHRH in human anterior pituitary tissues using RIAs specific for the C-terminus or the midportion of hGHRH-(1-44)-NH2, size-exclusion chromatog., HPLC, Western blotting, and immunocytochem. The anterior pituitary ir-forms were compared to those found in hypothalamus, posterior pituitary, and GHRH-secreting **endocrine** pancreatic tumors. Three ir-forms of hGHRH with mol. wt. of 30-45, 10, and 5 kDa were detected. The 30- to 45-kDa ir-form was very likely to consist of hGHRH bound to proteins. The 5-kDa ir-form represented mature forms of hGHRH. It was the major form in tissues actively synthesizing and/or secreting hGHRH. Nontumoral anterior pituitaries contained significant amts. of mature hGHRH. The 10-kDa form was identified as a hGHRH precursor ir-form. In addn. to its expected presence in the hypothalamus and GHRH-secreting **tumors**, normal and **tumoral** human anterior pituitaries contained an identical **ir**-form of the hGHRH precursor. Cells immunoreactive for the hGHRH precursor were obsd. in pituitary adenomas. Evidence for precursor and mature ir-forms of hGHRH in anterior pituitary tissues provides conclusive arguments for the endogenous synthesis of the neuropeptide.

L41 ANSWER 22 OF 66 HCAPLUS COPYRIGHT 2000 ACS
AN 1995:744074 HCAPLUS
DN 123:192533
TI In vivo visualization of pituitary dopaminergic receptors by iodine-123 methoxybenzamide (IBZM) correlates with sensitivity to dopamine agonists in two patients with macroprolactinomas
AU Scillitani, A.; Dicembrino, F.; Di Fazio, P.; Vettori, P. Paleani; D'Angelo, V.; Scarabino, T.; Liuzzi, A.
CS Divisions of Endocrinology (A.S., A.L.) and Neurosurgery (V.D.), Istituto Di Ricovero e Cura A Carattere Scientific Co., 71013, Italy
SO J. Clin. Endocrinol. Metab. (1995), 80(8), 2523-5
CODEN: JCEMAZ; ISSN: 0021-972X
DT Journal
LA English
AB We performed in two patients with macroprolactinoma, pituitary

scintigraphy with 123-iodine-methoxybenzamide (IBZM), a dopaminergic antagonist that specifically binds to the D2 dopaminergic receptors. In a 34-yr-old woman with basal PRL levels of about 2000 n/mL, 7.5 mg/day of bromocriptine (Br) for a month neither reduced PRL levels nor affected **tumor** size; in this patient single **photon** emission tomog. SPECT failed to show any pituitary accumulation of the tracer. In the other patient, a 27-yr-old man presenting with cerebrospinal fluid rhinorrhea, basal PRL levels were at 5000 ng/mL; magnetic resonance imaging (MRI) demonstrated a huge pituitary tumor, and SPECT showed a very intense concn. of IBZM at the level of the adenoma. PRL levels fell dramatically to 530 n/gmL with only 2.5 mg/day of Br after 4 days; after 6 days with 7.5 mg/day Br, PRL levels were 63 ng/mL, and the patient underwent surgery to correct cerebrospinal fluid leakage. We conclude that, in these two patients, the pituitary scintigraphy with IBZM has given information on the d. of dopamine receptors on the adenoma and has correlated with the inhibitor effect of Br on PRL secretion. Whether this tool might be of value in identifying patients with pituitary tumors potentially responsive to Br treatment is still to be investigated.

L41 ANSWER 23 OF 66 HCAPLUS COPYRIGHT 2000 ACS
AN 1983:552648 HCAPLUS
DN 99:152648
TI **Photoperiodic** control of melanoma growth in hamsters: influence of pinealectomy and melatonin
AU Stanberry, L. R.; Das Gupta, T. K.; Beattie, C. W.
CS Dep. Surg., Univ. Illinois, Chicago, IL, 60680, USA
SO Endocrinology (Baltimore) (1983), 113(2), 469-75
CODEN: ENDOAO; ISSN: 0013-7227
DT Journal
LA English
GI



I

AB Pinealectomy (PX) increased MM1 (melanotic melanoma no. 1) hamster melanoma growth in animals held under a 14-h **light**, 10-h dark (14:10) **photoperiod** without altering **tumor** latency. Hamsters maintained under a 6 h light, 18-h dark (6:18) **photoperiod** exhibited gonadal collapse, a longer **tumor** latency, and slower **tumor** growth rate than animals held under 14:10. PX produced a further increase in tumor latency and a decrease in growth in these animals. In contrast, acute morning injection of low doses (50 .mu.g/day) of melatonin(I) or delivery by Silastic capsule (35 .mu.g/day) implanted at the time of tumor cell inoculation increased MM1 melanoma growth in hamsters held under 14:10 **photocycle**, without affecting testicular or adrenal function. Treatment of hamsters 11 wk

before tumor cell inoculation with 14 .mu.g/day I via Silastic capsule produced a decrease in serum **prolactin** (PRL) [9002-62-4] but no change in **tumor** growth or testicular or adrenal wts. in animals held under 14:10. Treatment of hamsters with 17.7 .mu.g/day I (Silastic capsule) 11 wk before tumor cell inoculation increased testes and adrenal wts. as well as serum PRL and androgen levels, but decreased **tumor** growth in hamsters held under a short daily **photoperiod.** Apparently, the **photoperiod** under which hamsters are maintained dictates the growth rate of MM1 tumors and the effect of PX on tumor behavior. When **photoperiod** alters gonadal and adrenal function, the quantity, time, and duration of I presentation are all important variables in the effect of melatonin on tumor growth.

L41 ANSWER 24 OF 66 HCAPLUS COPYRIGHT 2000 ACS
AN 1978:484807 HCAPLUS
DN 89:84807
TI Experimental chemo-, radio-, and **endocrine** therapy for human cancers transplanted in nude mice
AU Shimosato, Yukio; Kameya, Toru; Kubota, Tetsuro; Hirohashi, Setsuo; Hayashi, Hiroatsu; Ikeuchi, Shinji; Nagai, Kanji
CS Pathol. Div., Natl. Cancer Cent. Res. Inst., Tokyo, Japan
SO Proc. Int. Workshop Nude Mice (1977), 2, 499-508
CODEN: PIWMDW
DT Journal
LA English
AB Of 25 human tumors transplanted in nude mice, hepatic carcinoma, colon adenocarcinoma, and gastric carcinoma were inhibited by mitomycin C [50-07-7]. The **tumors** appeared to be less sensitive to **radiation** in nude mice than in humans. Breast **cancer** was dependent on estrogens but was not dependent on **prolactin.** These mice appeared to be valuable models for cancer chemotherapy.

L41 ANSWER 25 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 17
AN 1978:197519 BIOSIS
DN BA66:10016
TI HETEROGENEITY OF THE MTTW-15 MAMMO SOMATOTROPIC **TUMOR** PART 1 **LIGHT** MICROSCOPIC EVALUATION OF **CELL** TYPES BY MEANS OF IMMUNO CYTOCHEMISTRY MORPHOMETRIC QUANTITATION FLUORESCENCE CYTO **PHOTOMETRY** AND RADIO IMMUNOASSAY.
AU PARSONS J A; ERLANDSEN S L; CARPENTER A-M; DEBAULT L E
CS DEP. ANAT., UNIV. MINN. SCH. MED., MINNEAPOLIS, MINN. 55455, USA.
SO ANAT REC, (1978) 190 (3), 719-734.
CODEN: ANREAK. ISSN: 0003-276X.
FS BA; OLD
LA English
AB Large MtTW15 rat pituitary tumors produced 200- to 800-fold elevations in serum growth hormone (GH) and **prolactin** (PRL) levels. Female **tumor** host showed doubling in body weight, milk secretion and 2-fold hepatosplenomegaly. Pituitaries of host animals were reduced by about 50% in weight and concentrations of GH and PRL. Large tumors were well-encapsulated, multinodular and showed variable amounts of necrosis and hemorrhage. Cytofluorometric analysis revealed a range of 100-fold in nuclear DNA content of tumor parenchymal cells which were chromophobic, pleomorphic and frequently mitotic. Concentrations of hormones in tumors were less than in normal pituitaries and highly variable with the ratio of GH/PRL ranging up to 30-fold within the same tumor. Immunostaining and

linear scanning quantitation showed that about 50% of the tumor cells contained immunodetectable hormones. Comparison of immunostained adjacent sections showed that hormone-containing tumor cells were pleomorphic, unequally distributed within nodules, lacking distinctive identifying morphological characteristics and they contained GH or PRL but not both hormones simultaneously. Large MtTW15 tumors are comprised of a markedly heterogeneous population of tumor cells and the hormone-containing cells are monohormonal secreting tumor cells which can produce GH or PRL but not both hormones.

L41 ANSWER 26 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:349910 BIOSIS
DN PREV199800349910
TI Clinical results of 24 pituitary macroadenomas with linac-based stereotactic radiosurgery.
AU Yoon, Sei-Chul (1); Suh, Tae-Suk; Jang, Hong-Seok; Chung, Su-Mi; Kim, Yeon-Shil; Ryu, Mi-Ryeong; Choi, Kyu-Ho; Son, Ho-Yong; Kim, Moon-Chan; Shinn, Kyung-Sub
CS (1) Dep. Ther., Catholic Univ., Kangnam St. Mary's Hosp., No. 505 Banpo-Dong, Seocho-Ku, Seoul 137-040 South Korea
SO International Journal of Radiation Oncology Biology Physics, (July 1, 1998) Vol. 41, No. 4, pp. 849-853.
ISSN: 0360-3016.
DT Article
LA English
AB Purpose: To determine the impact of stereotactic radiosurgery (SRS) on the clinical course, hormonal status, and follow-up CT/MRI scan of pituitary macroadenomas. Methods and Materials: From July 1988 to March 1996, 24 pituitary macroadenomas had been treated using 6 MV linear accelerator based SRS. They consisted of 11 (45.8%) **prolactinomas**, 2 (8.3%) growth hormone (GH)-secreting **tumors**, 1 (4.2%) Cushing's disease, 8 (33.3%) nonsecreting (nonfunctioning: NF) **tumors**, and 2 (8.3%) mixed **prolactin**-growth hormone (PRL-GH)-secreting **tumors** (M:F = 12:12; aged 21-61 years). Postoperative irradiation was performed in all cases except for the instance of Cushing's disease. The prescribed dose to tumor center varied from 10 to 27 Gy (mean 21.1 Gy) using a collimator size of 0.5 to 2.5 cm. The follow-up duration ranged from 13 to 89 months (mean 49.2 months). Results from these patients were compared to our results using conventional radiation. Results: Visual acuity and field defect were improved or became normal in 19 (79.2%) cases. Four (16.7%) remained unchanged after the treatment. One (4.1%) progressed 6 years after SRS and subsequently had repeat surgery with conventional boost irradiation. Of the 13 (46.4%) **prolactinomas**, including two mixed PRL-GH secreting **tumors**, 11 (84.1%) revealed normal hormonal levels within 1 year after SRS. In contrast, it took 2 years to become normal after conventional **radiation** therapy. In four GH-secreting **tumors** including two mixed PRL-GH secreting tumors, SRS and conventional methods showed similar responses. On follow-up imagings of the 21 patients, the mass was completely resolved in 4 (16.7%), including 3 PR-Ls and one NF, decreased in 11 (45.8%), and unchanged in 5 (16.7%) with central necrosis or cysts. One (4.2%) progressed and was reoperated 6 years after treatment. The complications related to SRS were comparable to those from conventional method.

Conclusion: Radiosurgery can be used effectively in patients with pituitary adenoma. In this study, a more rapid hormonal and clinical response was achieved with radiosurgery than with conventional pituitary irradiation treatment.

L41 ANSWER 27 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:489967 BIOSIS
DN PREV199799789170
TI Apoptosis in human pituitary adenomas: A morphologic and in situ end-labeling study.
AU Kontogeorgos, George; Sambaziotis, Demetrios; Piaditis, George; Karameris, Andreas
CS Dep. Pathol., G. Gennimatas General Hosp. Athens, 154 Messogion Ave., 115 27 Athens Greece
SO Modern Pathology, (1997) Vol. 10, No. 9, pp. 921-926.
ISSN: 0893-3952.
DT Article
LA English
AB Apoptosis seems to be an important process in normal tissues and in neoplastic lesions. Although electron microscopic features of apoptosis are characteristic, it is difficult to detect apoptotic **cells** with accuracy by **light** microscopy. Labeling of intranucleosomal DNA fragmentation can provide information on the apoptotic status of tumors. We studied apoptosis by the in situ end-labeling technique in 85 pituitary adenomas (63 functioning, 22 nonfunctioning). The functioning **tumors** included 19 somatotroph, 17 lactotroph, 9 mixed growth hormone/**prolactin**-producing, 2 thyrotroph, and 16 corticotroph adenomas. A few scattered cells displaying characteristic apoptotic changes were observed by histologic examination and electron microscopy. We estimated the apoptotic labeling index (ALI) of the adenomas by quantitating the percentages of positive nuclei. Overall, functioning adenomas showed a significantly higher ALI (5.64%) than did nonfunctioning tumors (1.84%). The ALI was higher in thyrotroph adenomas (10.26%) and lower in corticotroph (5.94%), somatotroph (5.51%), lactotroph (5.25%), and mixed growth hormone/prolactin-producing adenomas (5.11%). In conclusion, in situ end-labeling showed that apoptosis mostly occurs in functioning pituitary adenomas. These data suggest that assessment of apoptosis can be used to evaluate drug effects and to define which adenoma subtypes are more susceptible to drug therapy.

L41 ANSWER 28 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:119802 BIOSIS
DN PREV199799426305
TI Pituitary carcinoma: A clinicopathologic study of 15 cases.
AU Pernicone, Peter J.; Scheithauer, Bernd W. (1); Sebo, Thomas J.; Kovacs, Kalman T.; Horvath, Eva; Young., William F., Jr.; Lloyd, Ricardo V.; Davis, Dudley H.; Guthrie, Barton L.; Schoene, William C.
CS (1) Dep. Lab. Med., Mayo Clin., 200 First St. SW, Rochester, MN 55905 USA
SO Cancer, (1997) Vol. 79, No. 4, pp. 804-812.
ISSN: 0008-543X.
DT Article
LA English
AB BACKGROUND: Pituitary carcinomas are rare adenohypophysial neoplasms, the definition, diagnosis, therapy, and prognosis of which are controversial.

METHODS. Pituitary carcinomas were defined as primary adenohypophysial neoplasms with documented craniospinal and/or systemic metastases. The authors report a clinicopathologic study of 15 examples examined by **light** microscopy, immunohistochemistry, and image analysis. Both proliferative activity and p53 **tumor** suppressor gene expression were studied. RESULTS: The study group consisted of 15 patients, including 8 males and 7 females ranging in age from 34-71 years (mean, 56 years). Of these patients, seven had adrenocorticotropic hormone (ACTH)-producing **tumors** (four in the context of Nelson's syndrome), seven had **prolactin**-producing **tumors**, and one had a nonfunctioning **tumor**. No evidence of diabetes insipidus was seen in any case. Fourteen tumors were initially considered macroadenomas. Of the ten cases for whom tumor extent was known, all had invasive tumors. The interval from the initial diagnosis of adenoma to that of carcinoma ranged from 0.3 to 18.0 years (mean, 6.6 years; median, 5.0 years); the longest mean interval (15.3 years) occurred for patients with Nelson's syndrome. The latency was twice as long for ACTH-producing **tumors** as for **prolactin** (PRL) cell **tumors** (9.5 vs. 4.7 years). All carcinomas showed a greater tendency toward systemic metastasis than craniospinal metastasis; the rate of systemic metastasis was 71% for PRL cell tumors and 57% for ACTH producing tumors. Thirteen percent of tumors showed both patterns of metastasis. Fully 50% of primary tumors and the majority of metastases showed nuclear pleomorphism and/or hyperchromasia. The mean mitotic, MIB-1, and proliferating cell nuclear antigen indices for primary tumors and metastases were as follows: 2/10 high-power field (hpf), 2.6% and 11%, respectively; 6/10 hpf, 7.8% and 16%, respectively. Staining for p53 protein was noted in 57% of primary tumors and 88% of metastatic tumors; a relative increase in p53 expression in metastases was noted in 83%. All but one of the primary and metastatic **tumors** were aneuploid. The most common treatments were **radiation** therapy and, for PRL **cell** carcinomas, dopamine agonist administration. Both treatments provided only palliation. Eighty percent of the patients died of metastatic disease 7 days to 8 years after the diagnosis of carcinoma; of these, 66% died within 1 year. At last follow-up, 20% of patients were alive with metastases 9-18 months after diagnosis. CONCLUSIONS: Nearly all pituitary carcinomas present as functioning, microscopically atypical or mitotically active, invasive macroadenomas. By definition, after an interval related to their immunotype, all metastasize. The tumors show a greater tendency toward systemic metastasis than craniospinal metastasis and are associated with poor prognosis. Radiation and dopamine agonist therapy generally provide only palliation. Proliferation indices and p53 expression tend to be higher in metastases than in primary tumors. The current definition of pituitary carcinoma requires the demonstration of metastasis; however, high mitotic and MIB-1 labeling indices as well as p53 immunoreactivity suggest the diagnosis and appear to be of prognostic significance. A redefinition of aggressive pituitary rumors is proposed-one that facilitates the recognition of tumors prone to metastasis.

L41 ANSWER 29 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1997:22360 BIOSIS
DN PREV199799321563
TI Hemorrhagic pituitary adenomas of adolescence.

AU Poussaint, Tina Young; Barnes, Patrick D.; Anthony, Douglas C.; Spack, Normal; Scott, R. Michael; Tarbell, Nancy J.
CS Dep. Radiol., Children's Hosp., 300 Longwood Ave., Boston, MA 02115 USA
SO AJNR, (1996) Vol. 17, No. 10, pp. 1907-1912.
ISSN: 0195-6108.
DT Article
LA English
AB PURPOSE: To review the clinical and MR imaging findings in adolescents with hemorrhagic pituitary adenomas and to compare those findings with pathologic results and outcome. METHODS: We reviewed the clinical records, imaging examinations, surgical and pathologic findings, and follow-up studies in 11 girls and six boys (12 to 20 years old; mean age, 16 years) with pituitary adenomas who were treated at our institution between August 1986 and June 1995. RESULTS: Of the 17 adenomas, eight were macroadenomas (gt 1 cm) in patients 14 to 18 years old (three girls, five boys). Six of the macroadenomas were grossly hemorrhagic, and appeared as high-intensity intrasellar/suprasellar masses on all MR sequences obtained before definitive diagnosis and treatment. Clinical presentation in the patients with the hemorrhagic macroadenomas included headache (five), visual field deficits (three), and neuroendocrine symptoms (three). One patient was asymptomatic. The preliminary clinical and imaging diagnoses were craniopharyngioma or Rathke's cyst in five of the six cases. Pathologic diagnoses were **prolactinoma** in four patients, plurihormonal (**prolactin**/follicle-stimulating hormone) **tumor** in one patient, and nonfunctioning adenoma in one patient. Surgical resection was performed in all six hemorrhagic **tumors** and **radiation** therapy was required in three cases. CONCLUSION: Pituitary adenomas uncommonly occur in childhood and are usually seen in adolescence. The majority of the macroadenomas are hemorrhagic and often occur in male subjects. The clinical and MR imaging features may mimic craniopharyngioma or Rathke's cyst. These **tumors** often require surgery and/or **radiation** therapy.

L41 ANSWER 30 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1996:540324 BIOSIS
DN PREV199699262680
TI Differentiating neuroblastoma of pituitary gland: Neuroblastic transformation of epithelial adenoma cells: Case report.
AU Lach, Boleslaw (1); Rippstein, Peter; Benoit, Brien G.; Staines, William
CS (1) Dep. Lab. Med., Div. Pathol., Ottawa Civic Hosp., 1053 Carling Ave., Ottawa, ON K1Y 4E9 Canada
SO Journal of Neurosurgery, (1996) Vol. 85, No. 5, pp. 953-960.
ISSN: 0022-3085.
DT Article
LA English
AB The authors report the case of a 40-year-old woman with a 12-year history of irregular menses, amenorrhea, infertility, galactorrhea, a slightly elevated prolactin level, and a slowly growing pituitary adenoma. She developed recent onset of visual symptoms, prompting craniotomy for removal of an intrasellar **tumor**. Following surgery, her vision and **prolactin** levels returned to normal. **Light**

microscopic and immunohistochemical examination of the **tumor** revealed it to be a neuroblastoma, which was immunohistochemically positive for synaptophysin, S-100 protein, and oxytocin. The **neoplasm** contained **prolactin**-positive neuroblastic and pituitary epithelial cells. No other pituitary hormones were found. Electron microscopy demonstrated two cell types: one with frequent neuritic processes containing neurosecretory granules and showing synaptic specialization, and another one compatible with epithelial adenohypophyseal cells. A few cells had ultrastructural features that were transitional between neuronal cells and granulated epithelial cells. Agranular folliculostellate cells were also identified. Immunoelectron microscopy demonstrated prolactin granules in the cytoplasm of the epithelial cells, in a few transitional cells, and in scattered neuritic processes. Ultrastructural and immunohistochemical features of the tumor suggested a transformation of pituitary epithelium to neuroblastic cells. Hyperprolactinemia and associated clinical symptoms may in part be attributed to selective **prolactin** secretion by **neoplastic** cells that were differentiating into adenomatous pituitary cells and, to a lesser extent, to cells differentiating into a neuroblastic line. Compression of pituitary stalk might also have been a contributory factor to the increased prolactin levels. Moreover, the oxytocin produced by the neuroblastic cells was considered an additional stimulus for **prolactin** secretion by **neoplastic** cells or by the normal pituitary.

L41 ANSWER 31 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:440511 BIOSIS
DN PREV199598454811
TI Estradiol-17-beta as an initiation modifier for **radiation**-induced mammary **tumorigenesis** of rats ovariectomized before puberty.
AU Inano, Hiroshi; Yamanouchi, Hiroshi; Suzuki, Keiko; Onoda, Makoto; Wakabayashi, Katsumi (1)
CS (1) Inst. Mol. Cell. Reg., Gunma Univ., Maebashi 371 Japan
SO Carcinogenesis (Oxford), (1995) Vol. 16, No. 8, pp. 1871-1877. ISSN: 0143-3334.
DT Article
LA English
AB This investigation evaluated the roles of estradiol-17-beta, progesterone and **prolactin** in the initiation of mammary **tumorigenesis** by irradiation. Sixty day old Wistar-MS rats ovariectomized bilaterally at 23 days of age were injected daily with olive oil, estradiol-3-benzoate (E-2B), progesterone or haloperidol for 14 days, and were then irradiated with gamma-rays (260 cGy) on the morning following the last injection. Diethylstilbestrol pellets were administered by implantation 30 days after the irradiation. Following treatment with E-2B, the incidence of mammary tumors was increased 2.2-fold, in comparison with that in the corresponding control rats. Bilateral ovariectomy before puberty caused the mammary glands of adult rats to atrophy, and a low degree of differentiation with long narrow ducts was observed in whole mounts. The DNA synthesis in the mammary glands and serum prolactin level of E-2B-treated rats were markedly increased and the terminal ducts showed distinctly increased differentiation into terminal end buds and alveolar

buds with prolactin receptors. When progesterone another ovarian hormone, or haloperidol, a dopamine antagonist in adenohypophysis, was injected into the rats under estrogen-free conditions, neither expression of prolactin receptors nor stimulation of DNA synthesis was observed in the mammary glands, and the incidence of mammary tumors induced by irradiation was lower than that observed in rats treated with E-2B. Combined treatment with E-2B and progesterone resulted in a reduction in the incidence of mammary **tumors** and in serum **prolactin** levels compared with those in E-2B alone, in spite of the synergistic effects on prolactin receptor concentration and DNA synthesis by the two hormones. On the other hand, concurrent administration of haloperidol did not reduce the E-2B-induced **tumor** incidence or **prolactin** concentration in serum. Many of the mammary **tumors** which developed in the ovariectomized rats were of the ER(-)PgR(-) type. The incidence of development of ER(+)PgR(+) tumors was increased by treatment with E-2B before the irradiation, and no ER(-)PgR(-) tumors were observed in this group. Our results suggest that estrogen is a direct or indirect sensitizer for **tumor** initiation by **radiation**, and is also one of the regulatory factors for hormone dependence of **radiation**-induced mammary **tumors**.

L41 ANSWER 32 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:219285 BIOSIS
DN PREV199598233585
TI Membrane estrogen receptors identified by multiple antibody labeling and impeded-ligand binding.
AU Pappas, Todd C.; Gametchu, Bahiru; Watson, Cheryl S. (1)
CS (1) Route F-45, Dep. Human Biol. Chem. Genet., Univ. Texas Med. Branch, Galveston, TX 77555-0645 USA
SO FASEB Journal, (1995) Vol. 9, No. 5, pp. 404-410.
ISSN: 0892-6638.
DT Article
LA English
AB GH-3/B6 rat pituitary **tumor** cells exhibit rapid **prolactin** release (within 5 min) when treated with nanomolar amounts of estrogen. However, the putative protein mediator of this nongenomic action has not been described. Using antibodies directed against a peptide representing the hinge region of the intracellular estrogen receptor (iER), we have demonstrated that these cells contain a membrane ER (mER). We now report that confocal scanning **laser** microscopy of **cells** labeled live with the anti-peptide antibody further supports a membrane localization of ER. The monoclonal antibodies H226 and H222 and a polyclonal antibody, ER21, each recognizing a unique epitope on iER (NH-2 terminal to the DNA-binding region, within the steroid binding region, and the NH-2-terminal end, respectively), also immunohistochemically label membrane proteins of immuno-selected GH-3/B6 cells. These cells also specifically bind a fluorescent estrogen-BSA conjugate. Coincubation of cells with anti-ER antibody and the fluorescent estrogen-BSA conjugate reveals that these labels colocalize on cells. These results suggest that mER may be structurally similar to iER.

L41 ANSWER 33 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS

AN 1993:230443 BIOSIS
DN PREV199395121618
TI Carcinogenic effect of in utero californium-252 and cobalt-60 irradiation in C57BL/6NXC3H/He F1 (B6C3F1) mice.
AU Nitta, Yumiko (1); Kamiya, Kenji (1); Yokoro, Kenjiro
CS (1) Dep. Pathology, Res. Inst. Nuclear Med. Biology, Hiroshima Univ., 1-2-3, Kasumi, Minami-Ku, Hiroshima 734 Japan
SO Journal of Radiation Research, (1992) Vol. 33, No. 4, pp. 319-333. ISSN: 0449-3060.
DT Article
LA English
AB C57BL/6N times C3H/He F1 mice were exposed in utero to 0, 1.0 and 2.7 Gy of 252Cf or 60Co at day 16.5th of gestation. Mice of both sexes were observed for 2 years. The females in the irradiated groups showed increases in the incidences of pituitary, mammary gland, liver and lung tumors. 252Cf was more effective in inducing tumors than was 60Co. Interestingly, the incidence of hematopoietic tumors decreased by irradiations with 252Cf but not with 60Co. The incidences of liver tumors in males increased by 252Cf-irradiation, whereas, the incidences of skin and soft tissue tumors increased by 60Co-irradiation. These results indicate that irradiation in utero during the late embryonic stage can induce tumors postnatally after a long latency. Moreover, females irradiated in utero had disfunction of the ovaries, evidence of impairment of the female's specific hormonal environment. This may be the cause of the low incidence of ovarian tumors and the high incidences of liver, lung and pituitary tumors in these female mice. Females with pituitary **tumors** had a high serum **prolactin**, which might be responsible for the concurrence of mammary gland **tumors**. These results indicate the importance of host factors in the development of **radiation**-induced **tumors**.

L41 ANSWER 34 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1991:343928 BIOSIS
DN BA92:43303
TI EFFECT OF DOPAMINE AGONIST MEDICATION ON PROLACTIN PRODUCING PITUITARY ADENOMAS A MORPHOLOGICAL STUDY INCLUDING IMMUNOCYTOCHEMISTRY ELECTRON MICROSCOPY AND IN-SITU HYBRIDIZATION.
AU KOVACS K; STEFANEANU L; HORVATH E; LLOYD R V; LANCRANJAN I; BUCHFELDER M; FAHLBUSCH R
CS DEP. PATHOL., ST. MICHAEL'S HOSP., 30 BOND ST., TORONTO, ONTARIO, M5B 18, CAN.
SO VIRCHOWS ARCH A PATHOL ANAT HISTOPATHOL, (1991) 418 (5), 439-446. CODEN: VAAHDJ. ISSN: 0174-7398.
FS BA; OLD
LA English
AB Conventional light microscopy, immunocytochemistry, electron microscopy and in situ hybridization were used to evaluate the effect of dopamine agonists (bromocriptine-LAR and bromocriptine) on the morphology of surgically removed prolactin (PRL)-producing pituitary adenomas. Dopamine agonist therapy resulted in decrease of serum PRL, clinical improvement and **tumor** shrinkage. Using **light** and electron microscopy cellular atrophy, interstitial and perivascular fibrosis were noted; in several tumors connective tissue accumulation was pronounced. The cellular response was not uniform. In some adenomas populations of large cells and small cells were distinguished. The large cells contained

immunoreactive PRL and expressed the PRL gene indicating resistance to dopamine agonists. It appears that these cells retained the potential to secrete PRL and proliferate despite exposure to dopamine agonists. In the small cells, PRL immunoreactivity and PRL gene expression decreased providing evidence that both PRL release and synthesis were blocked. Small cells can persist in tumors after discontinuation of dopamine agonist medication suggesting these small cells are irreversibly suppressed and are not capable of regaining their **endocrine** function and proliferative capability. The formation of irreversibly suppressed PRL cells may explain why some PRL-producing adenomas do not recur after withdrawal of dopamine agonists.

L41 ANSWER 35 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1992:212972 BIOSIS
DN BA93:113197
TI REGULATION AND MOLECULAR CHARACTERIZATION OF DOPAMINE D-2 RECEPTORS IN A **PROLACTIN**-SECRETING 7315A ANTERIOR PITUITARY **TUMOR**.
AU LEW J Y; ZAWADZKA H; FEIGENBLUM D; TANG D; FILER D; BENEDETTO P; GOLDSTEIN M
CS NEW YORK UNIV. MED. CENT., NEUROCHEM. RES. LAB., 560 FIRST AVE., ROOM H-544, NEW YORK, N.Y. 10016.
SO EUR J PHARMACOL MOL PHARMACOL SECT, (1990) 2 (6), 329-334.
CODEN: EJPPET. ISSN: 0922-4106.
FS BA; OLD
LA English
AB The regulation and molecular properties of the dopamine (DA) D2 receptors were compared in the **prolactin**-secreting 7315a anterior pituitary **tumor** with those in the striatum of rats. Chronic treatment with haloperidol increases the maximal binding for [3H]spiroperidol in tumor and striatum, but the percent increase is much higher in **tumor** than in striatum. **Photoaffinity** labelling of DA D2 receptors with N-(p-azido-m-[125]iodophenethyl)spiperone ([125I]N3-NAPS) yielded a major specifically labeled peptide with the Mr of 32-34 kDa in tumor, and two specifically labeled peptides with Mr of 32-34 and 92-94 kDa in striatum. The analysis of DA D2 receptor mRNA shows that the size is similar in tumor and striatum. The DA D2 receptor mRNA in tumor is very low and chronic treatment with haloperidol produces a considerable increase of the specific mRNA. It is postulated that the reported defect in regulation of prolactin release by DA agonists might be due to posttranslational changes in the tumor DA D2 receptor.

L41 ANSWER 36 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1986:321611 BIOSIS
DN BA82:45916
TI PITUITARY TUMOR CAUSING GIGANTISM MORPHOLOGY AND IN-VITRO HORMONE SECRETION.
AU ANNIKO M; RITZEN E M
CS DEPARTMENT OF OTOLARYNGOLOGY-HEAD AND NECK SURGERY, UNIVERSITY OF UMEA, S-901 85 UMEA, SWEDEN.
SO ORL (OTO-RHINO-LARYNGOL) (BASEL), (1986) 48 (3), 180-190.
CODEN: ORLJAH. ISSN: 0301-1569.
FS BA; OLD
LA English
AB True gigantism with overproduction of growth hormone (GH) and prolactin

(PRL) was diagnosed in a 13-year-old boy. The clinical history indicated that the tumour had caused an oversecretion of GH since the age of 4-5 years. At diagnosis,the sella turcica was markedly enlarged. No infiltrative growth was noted at surgery. **Endocrine** investigations showed elevated GH and PRL secretion. **Light** and electron microscopy of **tumour** tissue revealed densely packed pleomorphic **cells** of both GH and PRL type. In addition, oncocyte-like cells were observed. Organ culture of pieces of tumor tissue demonstrated continued secretion of GH and PRL into the medium for more than 5 days in vitro. Addition of bromocriptine to the medium caused a rapid decline in PRL secretion while GH secretion remained the same X-ray irradiation in vitro also caused a decrease in PRL secretion. These effects of bromocriptine and X-ray on hormone secretion in vitro mirrored the corresponding effect of treatment, when the patient showed signs of tumour recurrence after pituitary surgery. It is concluded that also in childhood, the in vitro response of tumour tissue to various treatment may be explored as a possible way to predict the efficacy of pharmacological or irradiation treatment of pituitary tumours.

L41 ANSWER 37 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1985:122716 BIOSIS
DN BR29:12712
TI PROGRESS IN **ENDOCRINE** RESEARCH AND THERAPY VOL. 1. SECRETORY TUMORS OF THE PITUITARY GLAND.
AU BLACK P M; ET AL
CS MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS.
SO BLACK, P. M. ET AL (ED.). PROGRESS IN ENDOCRINE RESEARCH AND THERAPY, VOL. 1. SECRETORY TUMORS OF THE PITUITARY GLAND. XV+400P. RAVEN PRESS: NEW YORK, N.Y., USA. ILLUS. (1984) 0 (0), XV+400P.
CODEN: PERTEZ. ISBN: 0-89004-585-2.
DT Book
FS BR; OLD
LA English
AB This inaugural volume of the series reviews the basic endocrinology and clinical management of pituitary tumors with known hormone secretions. The 4 main types of pituitary **tumors** are focused on in this book: **prolactinomas**, growth hormone-producing adenomas, adrenocorticotropin-producing adenomas and glycoprotein hormone-producing adenomas. Leading endocrinologists contribute articles on the regulation of **prolactin** secretion, **endocrine** diagnosis of **prolactin**-secreting pituitary **tumors**, effects of bromocriptine on **prolactinoma** morphology and the neurosurgical management of acromegaly. Further studies include corticotropin-releasing factor, endorphins in the normal and abnormal pituitary, medical management of Cushing's disease, and biosynthesis of the glycoprotein hormones. The book ends with 2 discussions on **light** and electron microscopic pathology of pituitary **tumors**, and surgical results for pituitary adenomas. The text is complemented with graphs, tables, extensive references and a subject index. This volume will interest all endocrinologists, neurologists, radiotherapists and other physicians who manage these tumors.

L41 ANSWER 38 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS

AN 1985:225730 BIOSIS
DN BA79:5726
TI EFFECT OF MELATONIN ON MAMMARY CARCINOGENESIS IN INTACT AND PINEALECTOMIZED RATS IN VARYING **PHOTOPERIODS**.
AU SHAH P N; MHATRE M C; KOTHARI L S
CS ENDOCRINOLOGY DIV., CANCER RESEARCH INSTITUTE, PAREL, BOMBAY 400012, INDIA.
SO CANCER RES, (1984) 44 (8), 3403-3408.
CODEN: CNREA8. ISSN: 0008-5472.
FS BA; OLD
LA English
AB Exposure of female Holtzman rats to constant light (24 h/day) immediately after birth significantly increased 9,10-dimethyl-1,2-benzanthracene-induced mammary cancer. Such functionally pinealectomized animals also revealed a significant increase in the circulating level of prolactin, and exaggerated development and proliferative activity of mammary epithelium as measured by quantitation of terminal end buds and alveolar buds from the whole mounts, and by DNA synthesis, respectively. Administration of melatonin (500 .mu.g/day per rat i.p. given from 52 to 145 days of age) completely abolished the effect of functional pinealectomy by sharply reducing 9,10-dimethyl-1,2-benzanthracene-induced cancer incidence from 95 to 25% during the post-9,10-dimethyl-1,2-benzanthracene observation period which lasted up to 180 days. Administration of melatonin to surgically pinealectomized animals exposed to constant **light** reversed the effect only partially by reducing the **cancer** incidence from 83 to 53%. Melatonin treatment in intact and surgically pinealectomized animals exposed to a short **photoperiod** revealed qualitatively similar differences in suppression of the **cancer** incidence. To have an impressive antitumor effect, presence of the pineal gland is essential, and the probable site of melatonin action appears to be at both the pineal gland and the hypothalamus.

L41 ANSWER 39 OF 66 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1978:135170 BIOSIS
DN BA65:22170
TI EFFECTS OF A GONADOTROPIN RELEASING HORMONE ANALOG A-43818 6-D LEUCINE 10 DEGLYCINAMIDE 9 PRO ETHYLAMIDE GONADOTROPIN RELEASING HORMONE ON 7 12 DI METHYL BENZ A ANTHRACENE INDUCED RAT MAMMARY TUMORS HISTOLOGICAL AND **ENDOCRINE** STUDIES.
AU DANGUY A; LEGROS N; HEUSON-STIENNON J A; PASTEELS J L; ATASSI G; HEUSON J C
CS LAB. HISTOL., FAC. MED., 97 RUE AUX LAINES, 1000 BRUXELLES, BELG.
SO EUR J CANCER, (1977) 13 (10), 1089-1094.
CODEN: EJCAAH. ISSN: 0014-2964.
FS BA; OLD
LA English
AB The effect of A-43818 [D-leu6 .**GRAPHIC**. pro-ethylamide9)]-GnRH was investigated on rats bearing 7,12-dimethylbenz(a)anthracene (DMBA)-induced mammary tumors. Tumor growth was significantly inhibited by the s.c. administration of 10 .mu.g A-43818, twice daily, for 6 wk. A dose of 25 .mu.g seemed less effective. Controls and experimental groups were subjected to radioimmunoassays (RIA) of serum luteinizing hormone (LH),

follicle-stimulating hormone (FSH) and prolactin (PRL), and histological examination of pituitaries and ovaries. Treatment with A-43818 resulted in atrophy of pituitary lactotropes and decreased prolactin concentration in plasma. Plasma LH levels were enhanced whereas FSH levels remained unchanged. The **endocrine** mechanisms of inhibition of **tumor** growth are discussed in the **light** of the well-known hormone dependance of DMBA-induced mammary **tumors**.

L41 ANSWER 40 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 87158561 EMBASE
DN 1987158561
TI Modification of expression of the malignant phenotype in **radiation**-initiated **cells**.
AU Gould M.N.; Watanabe H.; Kamiya K.; Clifton K.H.
CS University of Wisconsin-Madison, Department of Human Oncology, Madison, WI 53792, United States
SO International Journal of Radiation Biology, (1987) 51/6 (1081-1090). CODEN: IJRBA3
CY United Kingdom
DT Journal
FS 014 Radiology
022 Human Genetics
052 Toxicology
016 Cancer
LA English
AB Carcinogenesis is a multistage process consisting minimally of initiation and promotion/progression stages. Radiation and many environmental xenobiotics are potent initiating agents. We have shown that initiation of carcinogenesis in vivo by these agents is a common cellular event. In the irradiated thyroid (5 Gy) at least one in 20 **cells** is initiated. Initiation by both **radiation** and chemicals has also been shown to be a common cellular event in the mammary gland. Initiation therefore is most likely not the sole rate-limiting event in the carcinogenic process. The propensity of the initiated cell to express the malignant phenotype is modulated by many factors, including environmental chemicals and physiological and genetic factors. Scopal and abscopal physiological factors can either enhance or suppress the progression of initiated cells to a frank **tumour**. For example, **prolactin** enhances the rate of progression or **radiation** and chemically initiated mammary **tumours** while glucorticoids suppress this progression. TSH enhances the progression or **radiation**-initiated thyroid **tumours** while a scopal factor associated with unirradiated thyroid cells suppresses progression of this tumour type.

L41 ANSWER 41 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 87195694 EMBASE
DN 1987195694
TI Immunocytochemistry of pituitary tumors.
AU Heitz P.U.; Landolt A.M.; Zenklusen H.-R.; et al.
CS Department of Pathology, University of Basel, CH-4003 Basel, Switzerland
SO Journal of Histochemistry and Cytochemistry, (1987) 35/9 (1005-1011). CODEN: JHCYAS
CY United States
DT Journal

FS 003 Endocrinology
005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
016 Cancer
LA English
AB Pituitary **tumors** from 376 patients were investigated, using immunocytochemical techniques at the **light** and electron microscopic level, and autoradiography combined with immunocytochemistry for localizing somatostatin (SRIH) receptors. Prolactinomas, growth hormone-secreting adenomas causing acromegaly, and hormonally inactive adenomas were most frequently observed (153, 86, and 90 tumors, respectively). Among the latter, we could distinguish 'alpha-only adenomas,' many of which were oncocytomas. At the **light** and electron microscopic levels, **cells** containing (and presumably producing) simultaneously both prolactin and growth hormone, and cells containing exclusively either prolactin or growth hormone, could be demonstrated. In addition, a highly variable number and distribution of SRIH receptors could be shown in **tumors** secreting **prolactin**, growth hormone, and in **tumors** not associated with symptoms caused by inappropriate hormone secretion. The systematic combination of clinical, radiological, and biological techniques has currently brought great progress in the behavior and therapeutic concepts of pituitary lesions, and promises new achievements in the near future.

L41 ANSWER 42 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 87073999 EMBASE
DN 1987073999
TI Relationship between cellular morphology and immunocytological findings of
spontaneous pituitary tumours in the aged rat.
AU Nagatani M.; Miura K.; Tsuchitani M.; Narama I.
CS Hamamatsu Seigiken Research Laboratory Co., Hamamatsu, Shizuoka 344, Japan
SO Journal of Comparative Pathology, (1987) 97/1 (11-20).
CODEN: JCVPAR
CY United Kingdom
DT Journal
FS 005 General Pathology and Pathological Anatomy
003 Endocrinology
016 Cancer
020 Gerontology and Geriatrics
LA English
AB A total of 339 spontaneous pituitary **tumours** from 284 aged rats were studied by **light** microscopy. Based on the cellular morphology in preparations stained by haematoxylin and eosin, tumour cells
were classified into 4 types: (1) granular; (2) agranular small; (3) agranular large polygonal; and (4) agranular large slender cells. Eight tumours consisted of mixed neoplastic masses of 2 types of cells. A total of 85 cases representative for each tumour type was used for special staining and immunocytochemistry. All tumours of the granular cell type and some tumours of the agranular large polygonal cell type had granules which stained red by azocarmine and were positive for **prolactin**. All agranular small cell type **tumours** were also positive for **prolactin** and agranular slender cell type **tumours** were positive for adrenocorticotropic hormone. Only tumours of the agranular large polygonal cell type gave an indefinite or negative reaction for all

the various pituitary hormones. These results indicate a relatively good correlation between the cellular morphology and the immunocytochemistry of spontaneous pituitary tumours in aged rats.

L41 ANSWER 43 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 85056029 EMBASE
DN 1985056029
TI Prolactin cell carcinoma of the pituitary. Clinicopathologic, immunohistochemical, and ultrastructural study of a case with cranial and extracranial metastases.
AU Scheithauer B.W.; Randall R.V.; Laws Jr. E.R.; et al.
CS Department of Pathology, Mayo Clinic and Mayo Foundation, Rochester, MN 55905, United States
SO Cancer, (1985) 55/3 (598-604).
CODEN: CANCAR
CY United States
DT Journal
FS 016 Cancer
008 Neurology and Neurosurgery
003 Endocrinology
006 Internal Medicine
005 General Pathology and Pathological Anatomy
023 Nuclear Medicine
LA English
AB A patient with a primary adenohypophyseal **neoplasm** who had a long course marked by multiple surgical resections, **radiation** therapy, and high-dose dopamine agonist therapy developed local invasion as well as cranial and extracranial osseous metastatic lesions. The serum prolactin levels were greatly elevated, and immunohistochemical studies demonstrated **prolactin** in the cytoplasm of primary and metastatic **tumor** cells. Ultrastructural features of lactotrophic differentiation, including misplaced granule exocytosis, were observed. This is the third reported case of prolactin cell carcinoma that metastasized despite high-dose dopamine agonist therapy. Analysis of the patient's serum prolactin showed no abnormality in the chromatographic profile of biologic activity.

L41 ANSWER 44 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 86029890 EMBASE
DN 1986029890
TI Subarachnoid metastases from a prolactinoma.
AU Plangger C.A.; Twerdy K.; Grunert V.; Weiser G.
CS Department of Neurosurgery, University of Innsbruck, A-6020 Innsbruck, Austria
SO Neurochirurgia, (1985) 28/6 (235-237).
CODEN: NURABV
CY Germany
DT Journal
FS 008 Neurology and Neurosurgery
014 Radiology
016 Cancer
LA English
SL German
AB A 37-year-old man developed a left frontal metastasis from a **prolactin**-secreting pituitary **tumour**, which had been operated on nine years before. The metastatic tumor was totally excised.

One and a half years later he was found to have multiple left temporal and parietal subarachnoid metastases. Because treatment with bromocriptine for five months and subsequent **radiation** proved ineffective, the **tumour** nodules were removed surgically.

L41 ANSWER 45 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 85181638 EMBASE
DN 1985181638
TI Effects of bromocriptine on **prolactin**-secreting pituitary adenomas. Mechanism of reduction in **tumor** size evaluated by **light** and electron microscopic, immunohistochemical, and morphometric analysis.
AU Mori H.; Mori S.; Saitoh Y.; et al.
CS Department of Pathology, Medical School, Osaka University, Kita-ku, Osaka 530, Japan
SO Cancer, (1985) 56/2 (230-238).
CODEN: CANCAR
CY United States
DT Journal
FS 037 Drug Literature Index
016 Cancer
008 Neurology and Neurosurgery
003 Endocrinology
005 General Pathology and Pathological Anatomy
006 Internal Medicine
030 Pharmacology
LA English
AB Prolactin-secreting pituitary adenomas were studied to clarify the mechanism by which bromocriptine reduces tumor size. Patients examined consisted of three groups: Group I (four cases) received no medication, Group II (six cases) continued bromocriptine treatment (10 mg/day for 2 weeks) until the operation, and Group III (five cases) discontinued the treatment 1 week before the operation. Adenomas in Group II showed a variety of degenerative and necrotic changes of tumor cells in addition to marked decrease in volume of individual cell. Adenomas in Group III showed divergent structural changes. Irreversible changes seen in Group II became more pronounced with a marked increase in stromal tissue. Proliferative areas consisting of intermediate-sized cells were found in the scarce stromal tissue. The findings seem to indicate that the reduction in size of prolactinomas by bromocriptine treatment results from the reduction in size of individual tumor cell as well as from cell loss secondary to necrosis.

L41 ANSWER 46 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 85059634 EMBASE
DN 1985059634
TI Recurrent prolactinoma and meningioma following irradiation and bromocriptine treatment.
AU Kolodny J.; Dluhy R.G.
CS Endocrine-Hypertension Unit, Brigham and Women's Hospital, Boston, MA 02115, United States
SO American Journal of Medicine, (1985) 78/1 (153-155).

CODEN: AJMEAZ
CY United States
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
008 Neurology and Neurosurgery
006 Internal Medicine
014 Radiology
016 Cancer
030 Pharmacology
LA English
AB This case report describes a 45-year-old man with a massive extrasellar prolactinoma, treated initially with surgery and radiotherapy, who experienced a dramatic reduction of the bulk of his tumor but persistence and subsequent progression of an extrasellar portion while receiving long-term bromocriptine therapy, despite stable, suppressed **prolactin** levels. Although the residual **tumor** was thought to be adenomatous tissue unresponsive to bromocriptine, a meningioma was ultimately diagnosed. Because the meningioma may have been **radiation**-induced, clinicians are reminded to consider a second **neoplasm** in cases of apparent bromocriptine treatment failures, especially when **prolactin** levels are stable.

L41 ANSWER 47 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 85214736 EMBASE
DN 1985214736
TI Mesenchymal influences on the development of the adenohypophysis in the rat.
AU Schechter J.; Gash D.; Ahmad N.
CS Department of Anatomy and Cell Biology, University of Southern California School of Medicine, Los Angeles, CA 900333, United States
SO Cell and Tissue Research, (1985) 241/1 (67-76).
CODEN: CTSRCS
CY Germany
DT Journal
FS 008 Neurology and Neurosurgery
021 Developmental Biology and Teratology
LA English
AB Comparative studies have been made of development of the adenohypophysis using the Rathke's pouch (RP)-derived model system. Rathke's pouch with associated mesenchyme and ventral hypothalamus, was microsurgically isolated from 15-day fetal rats and placed in mild trypsin solution. Three variations of donor tissue were isolated and transplanted beneath the kidney capsule of adult hosts: A) pure pouch epithelium; B) pouch epithelium plus mesenchyme; and C) pouch epithelium with mesenchyme and ventral hypothalamus. After 30 days the grafts were isolated and processed for **light** and electron microscopy. **Cell** types were characterized by immunostaining as well as by morphological criteria. In group A well differentiated mammotrophs dominated the grafts, many of which were hypertrophied with widely dilated endoplasmic reticulum and Golgi saccules. Mammotrophs, frequently with mitotic figures, were distributed evenly throughout the grafts. Somatotrophs and gonadotrophs were neither abundant nor well differentiated in group A, but were both abundant and more extensively differentiated in groups B and C. Both somatotrophs and gonadotrophs were typically localized at margins of the

graft adjacent to connective tissue spaces. Well differentiated mammotrophs were present in groups B and C although there were fewer hypertrophied mammotrophs than in group A; and immunoreaction to **prolactin** was weaker than in group A. **Tumor**-like features found in all three groups included some loss of tissue integrity and large, vascular lakes unlined by endothelium. These findings suggest that differentiation of mammotrophs may be inhibited in part by mesenchyme associated with Rathke's pouch, since in the absence thereof these cells become hyperplastic. Conversely, differentiation of somatotrophs and gonadotrophs appears more dependent on these mesenchymal elements for normal development.

L41 ANSWER 48 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 86003534 EMBASE
DN 1986003534
TI A pituitary adenoma with dilated ventricles.
AU Mindel J.S.; Fetell M.R.
CS Department of Ophthalmology, Mount Sinai School of Medicine, New York, NY, United States
SO Survey of Ophthalmology, (1985) 30/1 (59-61).
CODEN: SUOPAD
CY United States
DT Journal
FS 012 Ophthalmology
008 Neurology and Neurosurgery
014 Radiology
003 Endocrinology
016 Cancer
LA English
AB It is generally accepted that postoperatively radiographic examinations be limited to the area of pathology. The patient presented here complained of visual difficulties two years after transphenoidal removal of a pituitary prolactinoma. His endocrinologist ordered what he believed to be the appropriate computed tomography study and the neuroradiologist did not correctly interpret the new finding of dilated ventricles. Subsequently, a second primary tumor was discovered, a pineal gland sarcoma. The patient had refused radiotherapy after removal of his **prolactinoma**. Had he not, his second **tumor** would probably have been attributed to **radiation**. It is interesting to speculate whether radiation scatter from treatment of the prolactinoma would have prevented the pineal gland sarcoma.

L41 ANSWER 49 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 85006597 EMBASE
DN 1985006597
TI A .mu.-opiate receptor in 7315c **tumor** tissue mediates inhibition of immunoreactive **prolactin** release and adenylate cyclase activity.
AU Frey E.A.; Kebabian J.W.
CS Experimental Therapeutics Branch, National Institute of Neurological and Communicative Disorders and Stroke, Bethesda, MD 20205, United States

SO Endocrinology, (1984) 115/5 (1797-1804).
CODEN: ENDOAO
CY United States
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
030 Pharmacology
040 Drug Dependence, Alcohol Abuse and Alcoholism
023 Nuclear Medicine
016 Cancer
LA English
AB **Cells** of the 7315c **tumor** released immunoreactive PRL (**IR**-PRL). Cholera toxin enhanced this release. Morphine and other opiate agonists inhibited **IR**-PRL release from both untreated and cholera toxin-treated **tumor cells**. The opiate-induced inhibition of **IR**-PRL release was concentration dependent and naloxone sensitive. Cholera toxin also enhanced the adenylate cyclase activity of 7315c tumor tissue. Opiates inhibited enzyme activity in both untreated and cholera toxin-treated 7315c tissue in a concentration-dependent and naloxone-sensitive manner. FK 33824 was more potent than [D-Ala2,D-Leu5]enkephalin in inhibiting IR-PRL release and adenylate cyclase activity. In cholera toxin-treated 7315c tumor tissue, GTP was required for opiate-induced inhibition of adenylate cyclase activity. Nonhydrolyzable analogs of GTP inhibited toxin-stimulated cyclase activity in the absence of an opiate. These results suggest that the 7315c tumor possesses a .mu.-opiate receptor; stimulation of this receptor inhibits both IR-PRL release and adenylate cyclase activity. An inhibitory guanyl nucleotide component may link the .mu.-opiate receptor to adenylate cyclase.

L41 ANSWER 50 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 84206737 EMBASE
DN 1984206737
TI Necrotic changes in prolactinomas after long term administration of bromocriptine.
AU Gen M.; Uozumi T.; Ohta M.; et al.
CS Department of Neurosurgery, Hiroshima University School of Medicine, Hiroshima, Japan
SO Journal of Clinical Endocrinology and Metabolism, (1984) 59/3 (463-470).
CODEN: JCEMAZ
CY United States
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
030 Pharmacology
016 Cancer
LA English
AB Six **prolactinoma** patients were studied endocrinologically and their **tumors** were examined histologically after long term bromocriptine therapy. In patient 1 with a large prolactinoma, a marked reduction in size and a remarkable decrease in elevated serum PRL levels occurred after bromocriptine treatment for 8 months. The histological findings consisted of two components, i.e. shrunken island-like cell nests and acellular spaces. Some degenerative and necrotic **tumor cells**, hyaline substance, and fibrosis were observed with

light and electron microscopy in these acellular spaces. Island-like **cell** nests consisted of atrophic cells having disproportionally scanty cytoplasm. The same histological findings were observed in four other patients. However, in another patient whose tumor decreased in size only slightly during bromocriptine therapy, the specimen had few acellular spaces. Thus, long term bromocriptine treatment of patients with prolactinomas may result in necrosis of some adenoma cells in some patients.

L41 ANSWER 51 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 83227392 EMBASE
DN 1983227392
TI Morphological changes in bromocriptine-treated pituitary tumours.
AU Anniko M.; Wersall J.
CS Dep. Otolaryngol., Karolinska Hosp., S-104 01 Stockholm, Sweden
SO Acta Oto-Laryngologica, (1983) 96/3-4 (337-353).
CODEN: AOLAAJ
CY Sweden
DT Journal
FS 037 Drug Literature Index
011 Otorhinolaryngology
016 Cancer
005 General Pathology and Pathological Anatomy
003 Endocrinology
008 Neurology and Neurosurgery
LA English
SL German
AB Eight cases of pituitary **tumours** (3 **prolactinomas**, 3 **tumours** secreting GH and 2 **tumours** with a concomitant secretion of GH and PRL) were treated prior to open surgery with bromocriptine. These cases emanated from a series of totally 128 operated cases with pituitary **tumours**. The **tumour** tissue was analysed by **light** and electron microscopy. In 4 cases severe morphological changes had occurred; minor changes were found in 4 cases. Specific morphological changes indicating a dysfunction effect had occurred in one case. It has not been possible to document any consistent finding with regard to tumour susceptibility to bromocriptine. In the present limited material, the extent of morphological damage could not be correlated to dose, duration of treatment period, or endocrinological type of tumour. Our 8 patients with tumours treated with bromocriptine prior to surgery were cases demonstrating no or unsatisfactory clinical/radiological effects of drug therapy.

L41 ANSWER 52 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 83179373 EMBASE
DN 1983179373
TI Aggressive pituitary tumor growth.
AU Anniko M.; Holm L.E.; Wersall J.
CS Dep. Otolaryngol., Karolinska Hosp., S-104 01 Stockholm, Sweden
SO Archives of Oto-Rhino-Laryngology, (1983) 238/1 (53-62).
CODEN: AORLCG
CY Germany
DT Journal
FS 011 Otorhinolaryngology

003 Endocrinology
016 Cancer
LA English
AB Three cases with extrasellar extension from our material of 132 pituitary **tumors** are reported. One **tumor** secreted growth hormone, one secreted **prolactin**, and one secreted adrenocorticotropic hormone (ACTH). All three patients had a short case history. The **tumors** recurred rapidly after surgery. **Light** microscopy showed pleomorphic **cells** but no signs of morphologic malignancy. Ultrastructural analysis revealed intracellular filamentlike inclusions, with a cross-banded substructure in two cases. The DNA analysis of two of the cases showed aneuploidy. Our three cases of pituitary tumors are likely to represent a particularly aggressive type of tumor growth.

L41 ANSWER 53 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82206483 EMBASE
DN 1982206483
TI Induction of **prolactin**-deficient variants of GH3 rat pituitary **tumor** cells by ethyl methanesulfonate: Reversion by 5-azacytidine, a DNA methylation inhibitor.
AU Ivarie R.D.; Morris J.A.
CS Dept. Mol. Popul. Genet., Univ. Georgia, Athens, GA 30602, United States
SO Proceedings of the National Academy of Sciences of the United States of America, (1982) 79/9 I (2967-2970).
CODEN: PNASA6
CY United States
DT Journal
FS 037 Drug Literature Index
022 Human Genetics
LA English
AB GH3 cells are a rat pituitary **tumor** line expressing two pituitary peptide hormones, **prolactin** (rPRL) and growth hormone. Recently, it was found that the DNA alkylating agent ethyl methanesulfonate can induce the appearance of rPRL-deficient GH3 cell variants at a high frequency (ca. 20-30%). As shown here, such variants cannot be induced at high frequency by irradiation of wild-type GH3 **cells** with **ultraviolet light**, indicating that the effect may be specific to treatment with alkylating agents. Furthermore, the DNA methylation inhibitor 5-azacytidine reverted an ethyl methanesulfonate-induced rPRL-deficient variant into rPRL-expressing cells at high frequency (ca. 50%). The revertants were stable for at least 30-35 generations. These results support the hypothesis that the alkylating agent may promote the specific methylation of the rPRL gene or a gene regulating its activity, either one of which leads to inactivation of expression of the rPRL gene in GH3 cells.

L41 ANSWER 54 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82217646 EMBASE
DN 1982217646
TI Cystic **prolactin** secreting **tumor**. A **light** microscopic, ultrastructual, and immunocytochemical study.
AU Kurisaka M.; Pearl G.S.; Takei Y.; Tindall T.
CS Dept. Neurol. Surg., Nihon Univ., Tokyo, Japan
SO Neurologia Medico-Chirurgica, (1982) 22/6 (453-460).

CODEN: NMCHBN
CY Japan
DT Journal
FS 008 Neurology and Neurosurgery
003 Endocrinology
005 General Pathology and Pathological Anatomy
026 Immunology, Serology and Transplantation
LA Japanese
SL English

L41 ANSWER 55 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82229296 EMBASE
DN 1982229296
TI Cerebrospinal fluid rhinorrhea: A complication of therapy for invasive prolactinomas.
AU Landolt A.M.
CS Dep. Neurosurg., Univ. Zurich, 8091 Zurich, Switzerland
SO Neurosurgery, (1982) 11/3 (395-401).
CODEN: NRSRDY
CY United States
DT Journal
FS 008 Neurology and Neurosurgery
037 Drug Literature Index
LA English
AB The majority of invasive prolactinomas can be predicted with a high probability if the preoperative **prolactin** level is above 2000 ng/ml. As these **tumors** cannot be extirpated radically, adjunctive **radiation** therapy is used to improve the results of treatment. On the basis of reports that bromocriptine induces tumor shrinkage and has an antimitotic effect, we combined adjunctive irradiation with bromocriptine therapy in 14 patients who had particularly extensive invasion. Two of these patients developed cerebrospinal fluid rhinorrhea 3 and 5 months, respectively, after the completion of radiation therapy. In both patients, the fistula was localized in the sellar region and was closed successfully. Rapid tumor shrinkage caused by irradiation combined with bromocriptine therapy may be a factor causing this complication; postoperative rhinorrhea is otherwise extremely rare in our surgical series. We also observed a third patient who did not have an operation, but who developed rhinorrhea after a course of irradiation and bromocriptine treatment. The periods of rhinorrhea coincided with periods of bromocriptine treatment.

L41 ANSWER 56 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 82084566 EMBASE
DN 1982084566
TI Structural changes in human pituitary tumor after bromocriptine therapy.
AU Rengachary S.S.; Tomita T.; Jefferies B.F.; Watanabe I.
CS Dept. Surg., Univ. Kansas Med. Cent. Coll. Health Sci. Hosp., Kansas City, KS, United States
SO Neurosurgery, (1982) 10/2 (242-251).
CODEN: NRSRDY
CY United States
DT Journal
FS 037 Drug Literature Index

008 Neurology and Neurosurgery
003 Endocrinology
014 Radiology
005 General Pathology and Pathological Anatomy
010 Obstetrics and Gynecology
LA English
AB The histological appearance of a **prolactin**-producing **tumor** and of a growth hormone-producing **tumor** after short term bromocriptine therapy was studied in detail using **light** microscopy with conventional and immunocytochemical methods and using transmission electron microscopy. The findings were correlated with clinical, radiological, and biochemical data. Histological changes consisting of clumping of nuclear chromatin and a marked reduction in cytoplasmic volume due to loss of ribosomes, rough endoplasmic reticulum, and Golgi complexes were observed only in the **prolactin** -producing **tumor**. Normalization of elevated serum **prolactin** levels and reduction in size of the **tumor** observed in serial computed tomograms correlated with striking histological changes found in the tumor. These changes were interpreted to represent a reversible inhibition of the protein-synthesis machinery of the neoplastic cell. Comparable clinical, biochemical, radiological, or structural changes were not observed in the growth hormone-secreting tumor.

L41 ANSWER 57 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 81110608 EMBASE
DN 1981110608
TI Cystic **prolactinoma**. A variant of 'transitional cell **tumor**' of the pituitary.
AU Pearl G.S.; Takei Y.; Kurisaka M.; et al.
CS Div. Neuropathol., Dept. Pathol., Emory Univ. Sch. Med., Atlanta, Ga. 30322, United States
SO American Journal of Surgical Pathology, (1981) 5/1 (85-90). CODEN: AJSPDX
CY United States
DT Journal
FS 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
023 Nuclear Medicine
003 Endocrinology
014 Radiology
LA English
AB Pituitary tumors with features of both Rathke's cleft cysts and adenohypophysial adenomas are extremely rare and have been termed 'transitional cell tumors'. The ultrastructural features of one of these tumors has been reported, demonstrating cells with features transitional between those of adenohypophysial cells and Rathke's cleft cells, along with other cells with the distinctive features of either cell type. We report a case of a **prolactin**-secreting 'transitional **cell tumor**' with similar **light**-microscopic and ultrastructural features. Additionally, the transitional **cells** in our case exhibited abundant intracellular mucin production. This represents a variant of the 'transient cell tumor' of the pituitary gland.

L41 ANSWER 58 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.

AN 81093112 EMBASE
DN 1981093112
TI Clinical and morphological findings in two cases of bromocriptine-treated prolactinomas.
AU Anniko M.; Wersall J.
CS Dept. ORL, Karolinska Sjukh., S-104 01 Stockholm 60, Sweden
SO Acta Pathologica et Microbiologica Scandinavica - Section A Pathology, (1981) 89/1 (41-47).
CODEN: AMBPBZ
CY Denmark
DT Journal
FS 005 General Pathology and Pathological Anatomy
016 Cancer
008 Neurology and Neurosurgery
037 Drug Literature Index
LA English
AB The morphology of 2 cases of **prolactin** (PRL) secreting pituitary **tumours** was analyzed at the **light** and electron microscopic level. Prior to surgery both patients had been treated with bromocriptine. In both tumours, groups of cells revealed considerable morphological changes but these were not confined to the whole adenoma. In fact, most cells still appeared ultrastructurally intact. Pieces from both adenomas were explanted to an in vitro system. These specimens secreted mainly PRL though smaller amounts of growth hormone (GH) were also produced. The cell morphology of the cultured specimens often showed a large number of preserved cells.

L41 ANSWER 59 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 80221659 EMBASE
DN 1980221659
TI **Prolactin**- and other hormone-producing pituitary **tumors** : **Radiation** therapy.
AU Noell K.T.
CS Duke Univ. Sch. Med., Durham, N.C., United States
SO Clinical Obstetrics and Gynecology, (1980) 23/2 (441-452).
CODEN: COGYAK
CY United States
DT Journal
FS 010 Obstetrics and Gynecology
003 Endocrinology
008 Neurology and Neurosurgery
014 Radiology
023 Nuclear Medicine
016 Cancer
029 Clinical Biochemistry
LA English
AB Determination of the radiotherapeutic treatment of choice for prolactinomas must await further clinical reports. Yttrium-90 implant therapy is clearly effective, and has been remarkably free of adverse effects, notably hypopituitarism, to date. Adverse results did occur with moderate frequency, however, in the larger groups of patients who received implants for other pituitary **tumors**. Conventional megavoltage irradiation can reduce **prolactin** levels, is relatively free of adverse effects as compared to other irradiation methods, and can be

considered as adjunctive therapy after surgery if **prolactin** hypersecretion persists or if suprasellar **tumor** extension occurs. The effectiveness of proton or alpha particle irradiation of prolactinomas is not yet known. These treatment methods are effective in the management of acromegaly and Cushing's disease. However, the incidence of adverse treatment effects suggests that hopes have not been fully realized that these methods would be less damaging to normal tissues. Conventional megavoltage irradiation remains a viable and competitive therapeutic method in the management of pituitary tumors.

L41 ANSWER 60 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 78412425 EMBASE
DN 1978412425
TI Male prolactin secreting pituitary adenomas in humans studied by peroxidase-labelled antibody method.
AU Osamura R.Y.; Watanabe K.; Teramoto A.; et al.
CS Dept. Pathol., Tokai Univ. Sch. Med., Boseida, Ischara City, Kanagawa, Japan
SO Acta Endocrinologica, (1978) 88/4 (643-652).
CODEN: ACENA7
CY Denmark
DT Journal
FS 003 Endocrinology
029 Clinical Biochemistry
006 Internal Medicine
016 Cancer
023 Nuclear Medicine
LA English
AB In order to identify the source of excess secretion of **prolactin** in male patients, the pituitary **tumors** of 11 males with hyperprolactinaemia were studied by peroxidase-labelled antibody method using antibodies against human **prolactin**. Using the **light** microscope, **prolactin** was demonstrated in most **tumor cells** in all cases. Ultrastructurally, **prolactin** was localized mainly on the secretory granules. Immunohistochemically positive cells were thought to correlate with the first type of tumor cells which were the major component observed by regular electron microscopic study without immunohistochemical staining. These findings indicated the secretion of an excess amount of **prolactin** by the **tumor** cells and were considered to be responsible for the category of Male Prolactin Secreting Pituitary Adenoma. The mechanism by which these male hyperprolactinaemic patients are endocrinologically non-functioning is also discussed.

L41 ANSWER 61 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 78267550 EMBASE
DN 1978267550
TI Galactorrhoea and hypogonadism associated with a radiologically inapparent **prolactin** secreting pituitary **tumour**.
AU McKenna T.J.; Glick A.D.; Cobb Jr. C.A.; Jacobs L.S.
CS Dept. Med., Vanderbilt Univ. Sch. Med., Nashville, Tenn. 37232, United States
SO Acta Endocrinologica, (1978) 87/2 (225-233).
CODEN: ACENA7
CY Denmark

DT Journal
FS 003 Endocrinology
008 Neurology and Neurosurgery
014 Radiology
006 Internal Medicine
016 Cancer
023 Nuclear Medicine
LA English
AB A 38 year old man was investigated because of impotence, gynaecomastia and galactorrhoea. Hyperprolactinaemia and hypogonadism were documented. Pituitary function was otherwise normal as was tomographic examination of the sella turcica. In the absence of direct evidence of pituitary involvement (hyperprolactinaemia can suppress gonadal function) and to exclude ectopic prolactin production, venous blood was drawn at multiple sites. The highest prolactin levels were found by RIA in the superior vena cava and above, indicating an intracranial source. At transsphenoidal hypophysectomy a microadenoma was removed; **tumour cells** contained typical **prolactin** secretory granules on electron microscopy. In the **light** of this report the appropriateness of dividing hyperprolactinaemia into '**tumorous**' and 'idiopathic' subgroups on the basis of sella size must be reconsidered. Functional tests do not distinguish between the subgroups although prolactin levels tend to be higher when the sella is enlarged. Only a quantitative rather than a qualitative difference may exist between the subgroups.

L41 ANSWER 62 OF 66 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
AN 79105020 EMBASE
DN 1979105020
TI Treatment of patients with prolactinomas.
AU Werder K.V.; Fahlbusch R.; Landgraf R.; et al.
CS Dept. Med., Innenstadt, Univ. Munich, Germany
SO Journal of Endocrinological Investigation, (1978) 1/1 (47-58).
CODEN: JEIND7
CY Italy
DT Journal
FS 037 Drug Literature Index
003 Endocrinology
010 Obstetrics and Gynecology
023 Nuclear Medicine
LA English
AB 51 female patients with **prolactin** producing **tumors** (PRL 1100 to 88,000 .mu.U/ml) and 26 male patients with **prolactin** producing **tumors** (PRL 6500 to 400,000 .mu.U/ml) were studied. Only 25% of the females had visual field defects which were present in 70% of the males. All females had amenorrhea but only 35 had galactorrhea. Hypopituitarism was rarely seen in the females but in most of the male patients. 24 females and all male patients were operated (transsphenoidal or transfrontal operation). PRL normalized in only eight females and in none of the males. Two patients became pregnant postoperatively, four after postoperative treatment with bromocriptine. Bromocriptine induced regular menses in 4 other patients operated by transsphenoidal route. Eight patients with microadenoma (PRL < 4000 .mu.U/ml) were treated with bromocriptine alone of whom two became pregnant. The males were also treated with bromocriptine leading to a significant fall of the PRL level

accompanied by improvement of libido, sexual potency and headache. Two patients received radiation postoperatively, which led to a fall of PRL and improvement of visual fields. Since PRL levels remained low after withdrawal of bromocriptine for several months an antiproliferative effect of this drug is suggested. Thus differential therapy of PRL producing tumors is possible: in females selective neurosurgery can alone or combined with medical therapy normalize PRL secretion and ovarian function. In patients with microadenoma bromocriptine alone can be successful. In patients with inoperable large **tumors** **radiation** should be advocated. Additional bromocriptine therapy may be helpful to stop tumor growth and alleviate the effects of hyperprolactinemia.

L41 ANSWER 63 OF 66 JICST-EPlus COPYRIGHT 2000 JST
AN 990768509 JICST-EPlus
TI Multiple **Endocrine** Neoplasia Type I Discovered after Remission of Invasive Thymoma. Report of a Case.
AU NAGAOKA SAKAE; BANDO TAKAFUMI; MASUDA RYO; ISOYAMA TOORU; FUJIMOTO YOSHIHIDE; TAKEMURA TAMIKO
CS Nissekiiryose
SO Gan no Rinsho (Japanese Journal of Cancer Clinics), (1999) vol. 45, no. 9, pp. 1012-1017. Journal Code: Z0928A (Fig. 5, Tbl. 1, Ref. 11) ISSN: 0021-4949
CY Japan
DT Journal; Short Communication
LA Japanese
STA New
AB A 38-year-old woman was admitted to our hospital because of a pancreatic tumor in July 1997. In 1992, an invasive thymoma had entered remission after chemoradiotherapy. Radiological examinations now revealed cystic tumors in the head and body of the pancreas and a solid tumor in the tail. Three islet-**cell** **tumors** were diagnosed and enucleation was done. **Light**-microscopic examination revealed that the cystic **tumors** in the head and body of the pancreas were covered with small, round cells and that the solid tumor in the tail consisted of the same type of cell in an eosinophilic stroma with calcification. The cystic tumors were immunohistochemically positive for glucagon, and the solid tumor was positive for insulin. Postoperative **endocrine** examinations showed high levels of intact parathyroid hormone and **prolactin**. The final diagnosis was multiple **endocrine** **neoplasia** type I with hyperparathyroidism, hyperpituitarism, and islet cell tumors. (author abst.)

L41 ANSWER 64 OF 66 JICST-EPlus COPYRIGHT 2000 JST
AN 920754831 JICST-EPlus
TI A Case of Prolactinoma Presenting with CSF Rhinorrhea and CSF Otorrhea during Bromocriptine Therapy.
AU NAKAJIMA TAKU; TAMURA TETSUO; KUROKI MIZUO; TANAKA RYUICHI HAYASHI HIROKO
CS Niigata Univ., Brain Res. Inst.
Niigata Univ., School of Medicine
SO Neurol Surg, (1992) vol. 20, no. 10, pp. 1091-1095. Journal Code: Z0684A (Fig. 3, Tbl. 1, Ref. 20)

ISSN: 0301-2603
CY Japan
DT Journal; Article
LA Japanese
STA New
AB Cerebrospinal fluid(CSF) leakage is a rare complication of prolactinoma treated with bromocriptine(BC). BC is known to be effective for reducing the volume of a prolactinoma and for decreasing the serum level of **prolactin**(PRL). In cases of pituitary **tumors**, CSF leakage is thought to be caused by shunting between the subarachnoid and extradural spaces. We had a case presenting with CSF rhinorrhea and CSF otorrhea during BC therapy which was treated successfully. The mechanism and treatment of CSF leakage were studied. A 55-year-old woman complaining of nasal obstruction and headache was admitted to our hospital on Nov. 22, 1988. CT scan showed a huge intracranial mass lesion involving the sella and the supra-sellar region and invading the sphenoid sinus and ethmoid sinus. Serum PRL level was 18,000ng/ml The patient was diagnosed as having an invasive prolactinoma, and BC therapy (5.0mg per day) was instituted. Three days later, CSF rhinorrhea developed, and BC treatment discontinued; **radiation** therapy was started. After 36Gy irradiation the size of the **tumor** was same on CT, and serum level of PRL was still high. The patient underwent trans-sphenoidal operation. The tumor was removed partially and the presumed CSF fistula was repaired. The sella and sphenoid sinus were packed with fat. BC treatment was reinstituted, and the serum PRL level decreased gradually without recurrent CSF rhinorrhea. Two weeks later the patient returned complaining of bilateral hearing disturbance. With a diagnosis of exudative otitis media she underwent bilateral tympanostomy. Immediately after tympanostomy, pulsating discharge from the middle ear was observed. The continuous discharge was serous, clear and glucosepositive. On CT scan, mastoid air cells and the middle ear bilaterally were of water density. A diagnosis of CSF otorrhea was made, and lumbar spinal drainage was started. (abridged author abst.)

L41 ANSWER 65 OF 66 JICST-EPlus COPYRIGHT 2000 JST
AN 890475101 JICST-EPlus
TI **Antitumor** effect of bromocriptine on **prolactin** -secreting pituitary **tumors**. Part 1. Pathological changes in rats **prolactinomas**.
AU SHIMA KATSUJI; KAMIYAMA JUNKO; CHIGASAKI HIROO; SEKI KATSUYOSHI ISHIKAWA JUNKO
CS National Defence Medical College
Boeiidai Kyodoriyokenshisetsu
SO Boei Ika Daigakko Zasshi (Journal of the National Defense Medical College), (1989) vol. 14, no. 1, pp. 46-52. Journal Code: Z0589A (Fig. 6, Ref. 24)
ISSN: 0385-1796
CY Japan
DT Journal; Article
LA Japanese
STA New
AB It is well known that bromocriptine(CB) inhibits **prolactin**(PRL) secretion and causes reduction in **tumor** size of PRL-secreting pituitary **tumors** (**prolactinomas**). However, the

mechanism of **antitumor** effect of CB is not fully understood. Experimental **prolactinomas** were induced in young adult female Sprague-Dawley rats by repeated subcutaneous injections of estradiol dipropionate (5mg/kg) at 2-week intervals for 12 weeks. Controls received an equivalent volume of sesame oil instead of estrogen. Twelve weeks after the first injection, estrogen-treated and control animals had daily subcutaneous injection of CB (1mg/kg) for 2 weeks. The effects of CB on the prolactinomas were determined by serum concentration of PRL, weight of pituitary gland, light microscopy, immunohistochemistry and electron microscopy. After the estrogen injection, the serum PRL levels increased strikingly, and the pituitaries increased in weight and showed adenomatous change. Immunohistochemistory showed that most tumor cells were positive for PRL. Electron micrographs showed well developed rough endoplasmic reticulum and Golgi apparatus. CB treatment reduced rapidly and markedly the serum PRL content and pituitary weight. **Light** micrographs showed an increase in eosinophilic **cells**. Electron micrographs showed reduced rough endoplasmic reticulum and Golgi apparatus in shrunk cytoplasma. These results indicates that CB has a direct action on the individual **tumor** cells of **prolactinomas** and thereby reduces the size of them.(author abst.)

L41 ANSWER 66 OF 66 CONFSCI COPYRIGHT 2000 CSA
AN 2000:3706 CONFSCI
DN 00-003706
TI Properly timed daily administration of **prolactin** enhances anti-**tumor** responses to **photodynamic** therapy
AU Cincotta, A.H.; Cincotta, E.; Cincotta, L.
CS Ergo Sci. Corp., Charlestown, MA, USA
SO Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 10016, USA; fax: 212-685-4540; email: www.dekker.com; URL: intellprop@dekker.com, Abstracts available. Contact Marcel Dekker for price..
Meeting Info.: 993 5027: Joint Meeting of 8th International Conference of Chronopharmacology and Chronotherapeutics and the American Association for Medical Chronobiology and Chronotherapeutics (9935027). Williamsburg, VA (USA). 24-28 Aug 1999. Rothschild Fdtn, Ambulatory Monitoring, Bayer, Elan, Ergo Science, Finkelstein, HealthPartners, Hoechst Marion Roussel, Marcel Dekker, McGovern Fund, Muro, Purdue Pharma, Rhone-Poulenc Rorer, Searle, Sepracor, Space Labs Medical, Univ TX - Houston.
DT Conference
FS DCCP
LA English

=> D 1-5 BIB ABS

L54 ANSWER 1 OF 5 MEDLINE
AN 94030679 MEDLINE
DN 94030679
TI In vitro study of the effect of **photodynamic** therapy on pituitary adenomas.
AU Marks P V; Buxton T; Furneaux C E
CS Department of Neurosurgery, General Infirmary at Leeds, UK.
SO BRITISH JOURNAL OF NEUROSURGERY, (1993) 7 (4) 401-6.
Journal code: AHZ. ISSN: 0268-8697.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199402
AB **Photodynamic** therapy (PDT) has been employed in the management of recurrent cerebral gliomas, but its activity against pituitary adenomas has not been specifically studied. An in vitro study of the effects of PDT against a variety of pituitary adenomas was conducted. It was found that PDT using haematoporphyrin derivative as a **photosensitizer** showed dose dependent activity against a variety of pituitary adenomas. The activity of PDT against pituitary adenomas should be investigated further and may hopefully provide a useful form of adjuvant therapy for preventing recurrence of micro-invasive pituitary adenomas or dealing with established recurrence after surgery and radiotherapy.

L54 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:227537 HCAPLUS
DN 132:262172
TI Use of neoangiogenesis markers for diagnosis and treatment of **tumors**
IN Krause, Werner; Muschick, Peter
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000018439	A2	20000406	WO 1999-EP7198	19990929
W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, ES, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
DE 19845798	A1	20000413	DE 1998-19845798	19980929

PRAI DE 1998-19845798 19980929
AB Neoangiogenesis markers (i.e. antibodies or receptors for e.g. vascular endothelial growth factor, placenta growth factor, acidic or basic FGF,

transforming growth factor .alpha. or .beta., hepatocyte growth factor, insulin-like growth factor I, glycoprotein B61, protein LERK-1, flk-1 receptor, etc.) or partial sequences thereof and antiangiogenic compds. and factors such as paclitaxel, endostatin, fibronectin peptide, and fumagillin are conjugated with active agents such as chemotherapeutic agents, radiosensitizers, **photosensitizers**, antibodies, oligonucleotides, radioactive metal complexes, etc., which may be bound to carriers, for treatment of **tumors**. Likewise, neoangiogenesis markers may be conjugated to diagnostic agents such as MRI, radiog., ultrasound, or near-IR contrast agents for **tumor** diagnosis. Thus, N',N',N''',N'''-tetrakis(tert-butoxycarboxymethyl)-N''-(hydroxycarboxymethyl)diethylenetriamine was converted to its N-hydroxysuccinimide ester, coupled to a Thy-1 antibody, complexed with 186Re, and injected i.v. into rabbits for detection of implanted VX2 **tumors** by scintigraphy with a gamma camera.

L54 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2000 ACS
AN 1997:740112 HCAPLUS
DN 128:11512
TI Growth inhibition and eradication of **tumors** using neuroendocrine resetting therapy and **photodynamic** therapy
IN Cincotta, Anthony H.; Cincotta, Louis
PA Ergo Science Incorporated, USA; General Hospital Corporation; Rowland Institute for Science
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9740829	A1	19971106	WO 1997-US7577	19970415
	W: CA, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 910365	A1	19990428	EP 1997-922668	19970415
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-16619 19960501
WO 1997-US7577 19970415
AB A method of ablating the growth of or eradicating **tumors** in mammals having **prolactin**, growth hormone, and melatonin daily rhythms involves adjusting one or more of the **prolactin**, growth hormone, and melatonin profiles of the mammal to conform to or approach the corresponding normal profile for healthy members of the same species and sex as said mammal, contacting the cells of the **tumor** with a **photoactive photosensitizer**, and, exposing the **photosensitizer**-contact **tumor** cells to light of a predetd. wavelength, power d., and energy level.

L54 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:461003 BIOSIS
DN PREV199800461003
TI Resetting the neuroendocrine-immune axis leads to enhanced PDT effects.
AU Cincotta, A.; Henion, J.; Cincotta, E.
CS Ergo Science Corp., Charlestown, MA 02129 USA

SO Photochemistry and Photobiology, (June, 1998) Vol. 67, No. SPEC. ISSUE, pp. 92S.
Meeting Info.: 26th Annual Meeting of the American Society for Photobiology Snowbird, Utah, USA July 11-15, 1998 American Society for Photobiology
. ISSN: 0031-8655.
DT Conference
LA English

L54 ANSWER 5 OF 5 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
AN 1997-549483 [50] WPIDS
DNC C1997-175200
TI Treatment of **tumours** - by adjusting the **prolactin** profile towards a normal profile using a **prolactin** enhancer or reducer, and using **photodynamic** therapy..
DC B02 B05
IN CINCOTTA, A H; CINCOTTA, L
PA (ERGO-N) ERGO RES CORP; (GEHO) GEN HOSPITAL CORP DBA MASSACHUSETTS GEN; (ROWL-N) ROWLAND INST SCI; (ERGO-N) ERGO SCI INC; (GEHO) GEN HOSPITAL CORP; (MASS-N) MASSACHUSETTS GEN HOSPITAL
CYC 21
PI WO 9740829 A1 19971106 (199750)* EN 44p
RW: AT BE CH DE DK ES FI FR GB GR IE IT LU MC NL PT SE
W: CA JP MX
EP 910365 A1 19990428 (199921) EN
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
ADT WO 9740829 A1 WO 1997-US7577 19970415; EP 910365 A1 EP 1997-922668 19970415, WO 1997-US7577 19970415
FDT EP 910365 A1 Based on WO 9740829
PRAI US 1996-16619 19960501
AN 1997-549483 [50] WPIDS
AB WO 9740829 A UPAB: 19971217
The following are claimed: e.g. (A) treating an mammal which has one or more **tumours**, where the mammal has a **prolactin** and a melatonin daily rhythm, comprising: (a) comparing the **prolactin** profile of the mammal to a normal **prolactin** profile for healthy animals of the same species and sex; (b) adjusting the **prolactin** profile of the mammal by administering **prolactin** enhancers or reducers, so that the **prolactin** profile conforms to or approaches the normal **prolactin** profile; (c) contacting the **tumour** cells with a **photosensitiser**; and (d) exposing the **tumour** cells to light of a predetermined wavelength and power density and energy level.

USE- The processes may be used for control and inhibition of **tumour** growth.

ADVANTAGE- The processes give enhanced reduction in **tumour** growth and accelerated eradication of **tumours**. They do not show the debilitating effects associated with chemotherapeutic agents or ionising **radiation**. The effects of the treatment may persist long-term, even after the administration of enhancer (or reducer) and **photodynamic** therapy (PDT) has been discontinued.
Dwg.0/7

=> D HIS

(FILE 'HOME' ENTERED AT 12:54:02 ON 26 MAY 2000)

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, LIFESCI, WPIDS, JICST-EPLUS, PHIN, PHIC, BIOTECHDS, BIOBUSINESS, PROMT, CONFSCI, DRUGB' ENTERED AT 12:54:42 ON 26 MAY 2000

L1	181672	S PROLACTIN
L2	183	S L1 AND (PHOTOSENS? OR PHOTOACTIV? OR PHOTO(2A)SENSI?)
L3	753	S L1 AND (PHENOTHIAZIN? OR ETNBS OR BENZO(4A)PHENOTHIAZIN?)
L4	936	S L2 OR L3
L5	103	S L4 AND (TUMOR? OR ANTITUMOR?)
L6	18	S L4 AND (TUMOUR? OR ANTITUMOUR?)
L7	60	S L4 AND (CANCER? OR ANTICANCER?)
L8	97	S L4 AND (NEOPLAS? OR ANTINEOPLAS?)
L9	3	S L4 AND (SARCOM? OR ANTISARCOM?)
L10	187	S L5-L9
L11	3	S L10 AND (PHOTODYNAM? OR PHOTO OR LIGHT OR PDT)
L12	5	S L10 AND PHOTO?
L13	5	S L11 OR L12
L14	4	DUP REMOV L13 (1 DUPLICATE REMOVED)

Narrower approach to search

Searched by John Dantzman 703-308-4488

=> D 1-4 BIB ABS

L14 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 1
AN 1997:740112 HCAPLUS
DN 128:11512
TI Growth inhibition and eradication of **tumors** using neuroendocrine resetting therapy and **photodynamic** therapy
IN Cincotta, Anthony H.; Cincotta, Louis
PA Ergo Science Incorporated, USA; General Hospital Corporation; Rowland Institute for Science
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9740829	A1	19971106	WO 1997-US7577	19970415
	W: CA, JP, MX				
	RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	EP 910365	A1	19990428	EP 1997-922668	19970415
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-16619 19960501
WO 1997-US7577 19970415
AB A method of ablating the growth of or eradicating **tumors** in mammals having **prolactin**, growth hormone, and melatonin daily rhythms involves adjusting one or more of the **prolactin**, growth hormone, and melatonin profiles of the mammal to conform to or approach the corresponding normal profile for healthy members of the same species and sex as said mammal, contacting the cells of the **tumor** with a **photoactive photosensitizer**, and, exposing the **photosensitizer**-contact **tumor** cells to **light** of a predetd. wavelength, power d., and energy level.

L14 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2000 ACS
AN 2000:227537 HCAPLUS
DN 132:262172
TI Use of neoangiogenesis markers for diagnosis and treatment of **tumors**
IN Krause, Werner; Muschick, Peter
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000018439	A2	20000406	WO 1999-EP7198	19990929
	W: AE, AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CR, CU, CZ, DM, EE, ES, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
DE 19845798 A1 20000413 DE 1998-19845798 19980929
PRAI DE 1998-19845798 19980929
AB Neoangiogenesis markers (i.e. antibodies or receptors for e.g. vascular endothelial growth factor, placenta growth factor, acidic or basic FGF, transforming growth factor .alpha. or .beta., hepatocyte growth factor, insulin-like growth factor I, glycoprotein B61, protein LERK-1, flk-1 receptor, etc.) or partial sequences thereof and antiangiogenic compds. and factors such as paclitaxel, endostatin, fibronectin peptide, and fumagillin are conjugated with active agents such as chemotherapeutic agents, radiosensitizers, **photosensitizers**, antibodies, oligonucleotides, radioactive metal complexes, etc., which may be bound to carriers, for treatment of **tumors**. Likewise, neoangiogenesis markers may be conjugated to diagnostic agents such as MRI, radiog., ultrasound, or near-IR contrast agents for **tumor** diagnosis. Thus, N',N',N''',N'''-tetrakis(tert-butoxycarboxymethyl)-N''-(hydroxycarboxymethyl)diethylenetriamine was converted to its N-hydroxysuccinimide ester, coupled to a Thy-1 antibody, complexed with 186Re, and injected i.v. into rabbits for detection of implanted VX2 **tumors** by scintigraphy with a gamma camera.

L14 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1998:461003 BIOSIS
DN PREV199800461003
TI Resetting the neuroendocrine-immune axis leads to enhanced **PDT** effects.
AU Cincotta, A.; Henion, J.; Cincotta, E.
CS Ergo Science Corp., Charlestown, MA 02129 USA
SO Photochemistry and Photobiology, (June, 1998) Vol. 67, No. SPEC. ISSUE, pp. 92S.
Meeting Info.: 26th Annual Meeting of the American Society for Photobiology Snowbird, Utah, USA July 11-15, 1998 American Society for Photobiology
. ISSN: 0031-8655.
DT Conference
LA English

L14 ANSWER 4 OF 4 SCISEARCH COPYRIGHT 2000 ISI (R)
AN 92:77396 SCISEARCH
GA The Genuine Article (R) Number: HA626
TI SYNTHESIS AND CHARACTERIZATION OF A HIGH-AFFINITY **PHOTOACTIVATABLE** ANALOG OF THYROTROPIN-RELEASING-HORMONE
AU BRADY K D; TASHJIAN A H (Reprint)
CS HARVARD UNIV, SCH PUBL HLTH, TOXICOL LAB, 665 HUNTINGTON AVE, BOSTON, MA, 02115; HARVARD UNIV, SCH MED, DEPT BIOL CHEM & MOLEC PHARMACOL, BOSTON, MA, 02115
CYA USA
SO BIOCHEMICAL JOURNAL, (01 JAN 1992) Vol. 281, Part 1, pp. 179-184.
ISSN: 0264-6021.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 44
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB An analogue of thyrotropin-releasing hormone (TRH, pGlu-His-ProNH2),

i.e. pGlu-His-ProNH-(CH2)6-(4-azidosalicylamide) (TRH-ASA), has been synthesized and, in a radioiodinated form (TRH-IASA), characterized and used as a **photoaffinity** reagent to label the TRH receptor on rat pituitary GH4C1 cells. TRH-IASA bound to GH4C1 cells with high affinity (K(d) = 8 nM), comparable with that of TRH binding. The binding of TRH-IASA was competitive with binding of TRH, two TRH analogues and a TRH receptor antagonist, chlordiazepoxide. TRH-IASA did not bind to or label GH12C1 cells, which lack functional TRH receptors. Labelling of GH4C1 cells with TRH-IASA followed by SDS/PAGE and autoradiography of membrane proteins demonstrated labelling of a single polypeptide which ran as a diffuse band between 71 and 91 kDa, centered at 76 kDa. No change in this labelling pattern was observed as a function of the length of time (between 5 min and 2 h) that GH4C1 cells were incubated with 3 nM-TRH-IASA. Using either a very short (5 s) **photolysis** interval or low TRH-IASA concentrations, only the 76 kDa band was labelled. Minor bands appeared only after extended **photolysis** and use of high TRH-IASA concentrations. We conclude that the TRH receptor from rat pituitary GH4C1 cells is a single peptide with an apparent molecular mass of 76 kDa. Details of the chemical synthesis of TRH-ASA are given in Supplementary Publication SUP 50167 (5 pages), which has been deposited at the British Library Document Supply Centre, Boston Spa, Wetherby, West Yorkshire LS23 7BQ, U.K., from whom copies can be obtained on the terms indicated in Biochem. J. (1992) 281, 5.

=> d his

(FILE 'HOME' ENTERED AT 11:54:08 ON 26 MAY 2000)

FILE 'MEDLINE, HCAPLUS, BIOSIS, EMBASE, SCISEARCH, LIFESCI, WPIDS, JICST-EPLUS, PHIN, PHIC, BIOTECHDS, BIOBUSINESS, PROMT, CONFSCI, DRUGB' ENTERED AT 11:54:51 ON 26 MAY 2000

L1	157	S	CINCOTTA L?/AU
L2	402	S	CINCOTTA A?/AU
L3	37	S	L1 AND L2
L4	522	S	L1-L3
L5	186061	S	PROLACTIN?
L6	3	S	L3 AND L5
L7	146	S	L4 AND L5
L8	37	S	L3 OR L6
L9	16	DUP	REMOV L8 (21 DUPLICATES REMOVED)

Inventor search

=> d bib abs 1-16

L9 ANSWER 1 OF 16 MEDLINE DUPLICATE 1
AN 1999266306 MEDLINE
DN 99266306
TI Role of the immune system in mediating the antitumor effect of benzophenothiazine photodynamic therapy.
AU Hendrzak-Henion J A; Knisely T L; **Cincotta L**; Cincotta E; **Cincotta A H**
CS Ergo Science Corporation, Charlestown, MA 02129, USA.
SO PHOTOCHEMISTRY AND PHOTOBIOLOGY, (1999 May) 69 (5) 575-81. Journal code: P69. ISSN: 0031-8655.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199908
EW 19990802
AB The role of the host immune system in contributing to tumor regression following benzophenothiazine photodynamic therapy (PDT) was examined. Photodynamic therapy with 2-iodo-5-ethylamino-9-diethylaminobenzo[a]-phenothiazinium chloride (2I-EtNBS) eradicated EMT-6 mammary fibrosarcomas in 75-100% of treated mice. In contrast, PDT failed to inhibit tumor growth in T-cell-deficient nude mice. Furthermore, T-cell depletion studies with anti-CD8 antibody revealed that the CD8+ T-cell population was critical for an effective PDT response (tumor volume 14 days post-PDT: 262 mm3 vs 59 mm3 in controls; P < 0.01). Because anti-CD4 antibody inhibited tumor growth in the absence of PDT, the role of CD4+ T cells remains unclear. Depletion of natural killer (NK) cells in vivo with anti-asialo-GM1 antibody significantly reduced a suboptimal PDT effect relative to vehicle controls (tumor volume 13 days post-PDT: 513 mm3 vs 85 mm3, respectively; P < 0.001). However, splenic NK cells obtained from PDT-treated tumor-bearing mice were not cytotoxic in vitro against EMT-6 cells, suggesting that NK cells contribute to the PDT effect in vivo by an indirect mechanism. In addition, when mice with complete tumor regression following PDT were rechallenged 28 days later with 5 x 10(5) EMT-6 cells, tumor growth was significantly inhibited as compared to controls (tumor volume 40 days postrechallenge: 137 mm3 vs 833 mm3 in controls; P < 0.03; percent animals without tumor in five experiments: 67% vs 8% in controls). Collectively, these results demonstrate that CD8+ T cells are required to prevent tumor regrowth after 2I-EtNBS-PDT, NK cells contribute to this response and such PDT can elicit protective antitumor immunity.

L9 ANSWER 2 OF 16 MEDLINE DUPLICATE 4
AN 96226960 MEDLINE
DN 96226960
TI Benzophenothiazine and benzoporphyrin derivative combination phototherapy effectively eradicates large murine sarcomas.
AU **Cincotta L**; Szeto D; Lampros E; Hasan T; **Cincotta A H**
CS Rowland Institute for Science, Cambridge, MA 02142, USA.
SO PHOTOCHEMISTRY AND PHOTOBIOLOGY, (1996 Feb) 63 (2) 229-37.

Journal code: P69. ISSN: 0031-8655.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
EM 199610
AB The tumoricidal effects of photochemotherapy with two photosensitizers, 5-ethylamino-9-diethylaminobenzo[a] phenothiazinium chloride (EtNBS) and benzoporphyrin derivative monoacid ring A (BPD-MA), were evaluated separately and in combination against the EMT-6 fibrosarcoma implanted subcutaneously in BALB/c mice. Animals carrying tumors 8-10 mm in diameter were divided into eight different groups (approximately 20/group) and subjected to various photoirradiation and drug conditions. The tumor response to photodynamic therapy (PDT) was measured as the mean tumor wet weight 2 weeks post-PDT. The combination treatment with 5.25 mg/kg EtNBS and 2.5 mg/kg BPD-MA followed by photoirradiation with 100 J/cm2 at 652 nm and then by 100 J/cm2 at 690 nm resulted in a 95% reduction in the average tumor weights compared to controls (no light, no drugs) with 76% of the mice being tumor free 2 weeks post-PDT. Because treatment with EtNBS or BPD-MA at twice the light dose and drug concentration resulted in either no significant reduction in tumor weights or increased the lethality of treatment, respectively, the data suggest that the enhanced PDT effect observed with the combination of drugs is synergistic rather than additive. Histology of tumors 24 h post-PDT with the combination of drugs showed nearly complete destruction of the tumor mass with little or no damage to the vasculature and no extravasation of red blood cells. There was no damage to the normal skin adjacent to the tumor. Fluorescence microscopy of EMT-6 cells incubated in vitro with the two photosensitizers revealed that they were localized to different intracellular compartments. The fluorescence pattern from frozen tumor tissue slices following the in vivo administration of the photosensitizers indicated a greater intracellular localization for EtNBS vs BPD-MA.

L9 ANSWER 3 OF 16 MEDLINE DUPLICATE 5
AN 94163616 MEDLINE
DN 94163616
TI Novel photodynamic effects of a benzophenothiazine on two different murine sarcomas.
AU **Cincotta L**; Foley J W; MacEachern T; Lampros E; **Cincotta A H**
CS Rowland Institute for Science, Cambridge, Massachusetts 02142..
SO CANCER RESEARCH, (1994 Mar 1) 54 (5) 1249-58.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; Cancer Journals
EM 199406
AB The photochemotherapeutic properties of a novel benzophenothiazine, 5-ethylamino-9-diethylaminobenzo[a]phenothiazinium chloride, were assessed in vitro and in vivo against two murine mammary sarcoma models (EMT-6 and

RIF). Photodynamic therapy (PDT) of EMT-6 and RIF cells following a 30-min incubation with dye (0.4 microgram/ml) and a light dose of 3.3 J/cm2 killed 87.0 and 99.6% of the cells, respectively. Over this same time period, RIF cells accumulate more than twice the amount of dye than the EMT-6 cell line [7.54 +/- 0.17 (SD) versus 3.11 +/- 0.15 nmol/10(6) cells] which probably accounts for their increased sensitivity to PDT. Conversely, in vivo, the EMT-6 tumor accumulates 3 times more dye (34.66 +/- 2.16 micrograms/g dry weight) than the RIF tumor (12.28 +/- 1.27 micrograms of dye/g) 3 h post-s.c. injection of dye (15 mg/kg). A study of the concentration dependent uptake of dye (following s.c. injection) in the tumor and plasma of mice bearing the EMT-6 tumor indicated a nonlinear relationship for both compartments. Maximum tissue uptake of dye and discrimination between tumor and skin or muscle occur 3-8 h following s.c. injection of dye. The ratios of dye in the tumor to the dye in surrounding skin and gastrocnemius muscle 8 h following dye injection were 4:1 and 8:1, respectively. At 24 h after dye injection, the dye was not detectable by absorption spectroscopy in the tumor, skin, or muscle. Decreasing the fluence rate from 200 to 50 mW/cm2 at a total light dose of 100 J/cm2 optimized the PDT effect. At 3 h following s.c. administration of dye, PDT of EMT-6 (7.5 mg of dye/kg; 50 mW/cm2; 100 J/cm2) and RIF tumors (15 mg dye/kg; 50 mW/cm2; 150 J/cm2) resulted in 100 and 70% cures, respectively. Histology at 24 and 72 h post-PDT showed minimal or no damage to the surrounding tissue (skin) while 70-90% of the tumor cells were destroyed or damaged. Moreover, 50-60% of the tumor cells isolated and cultured immediately following PDT were found to be nonviable. Similarly, the administration of 60 mg 5-ethylamino-9-diethylaminobenzo[a]phenothiazinium chloride/kg also resulted in no damage to the skin 24 h following PDT. It is suggested that the redox properties of the dye coupled with the differing metabolic states of the tumor and skin, which increase the amount of photoactive, oxidized dye present in the tumor and decrease it in the skin, are responsible for this unique differential PDT effect.(ABSTRACT TRUNCATED AT 400 WORDS)

L9 ANSWER 4 OF 16 MEDLINE DUPLICATE 6
AN 93265457 MEDLINE
DN 93265457
TI Phototoxicity, redox behavior, and pharmacokinetics of benzophenoxazine analogues in EMT-6 murine sarcoma cells.
AU **Cincotta L**; Foley J W; **Cincotta A H**
CS Rowland Institute for Science, Cambridge, MA 02142.
SO CANCER RESEARCH, (1993 Jun 1) 53 (11) 2571-80.
Journal code: CNF. ISSN: 0008-5472.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Cancer Journals; Priority Journals
EM 199308

AB Structural modifications to the photoinactive benzophenoxazine Nile blue A
have led to three novel derivatives which include 5-ethylamino-9-diethylaminobenzo[a]phenoxazinium (EtNBA), 5-ethylamino-9-diethylaminobenzo[a]phenothiazinium (EtNBS), and 5-ethylamino-9-diethylaminobenzo[a]phenoselenazinium (EtNBSe) chlorides. The incorporation of sulfur and selenium into the benzophenoxazine moiety results in lipophilic, red-absorbing (650-660 nm) chromophores which possess significantly increased singlet oxygen yields (0.025 and 0.65, respectively, compared to 0.005 for EtNBA). This study examines the photosensitizing efficacies and pharmacokinetics in vitro in the EMT-6 murine mammary sarcoma cell line as well as the physicochemical, photochemical, and redox properties of these new analogues. Comparisons with Photofrin II, the only photosensitizer available clinically, were made in an attempt to high-light their different pharmacological characteristics. The photodynamic activity of the benzophenoxazine dyes correlates with their ability to generate the phototoxin singlet oxygen and increases in the following order: EtNBA < EtNBS << EtNBSe. At an extracellular dye concentration of 0.5 microM, the light dose required to kill approximately 50% of the cells was 2.0 and < 0.5 J/cm2 for the sulfur and selenium dyes, respectively. The light dose required to kill approximately 50% of the cells for both EtNBA and Photofrin II could not be determined because of their weak phototoxic effect under these conditions. At a light dose of 3.3 J/cm2, EtNBSe is approximately 1000 times more phototoxic than Photofrin II. All three benzophenoxazine derivatives are characterized by a similar uptake/efflux pattern in vitro consisting of a rapid and extensive cellular accumulation followed by a slow efflux rate. Contrary to their rapid uptake, 50% of the accumulated EtNBS and EtNBSe is retained intracellularly after a 6-h period in dye-free medium. Video-enhanced fluorescence microscopy corroborates the rapid uptake measurements as well as indicating the intracellular localization of the dyes in both living and thermally inactivated cells. Low extracellular dye concentrations (0.05 microM) result in a punctate fluorescence pattern in the perinuclear region, while higher dye concentrations (> 0.1 microM) lead to additional fluorescence in the cytoplasm, cytomembranes, and other organelles but apparently not the nucleus. Absorption spectrometry revealed that living cells rapidly reduce the dyes to their colorless leuko form (photoinactive) if oxygen is not readily available in the environment. It is shown that the cellular reduction is an enzymatic process and that an oxygen-free and cell-free medium containing both the coenzyme NADH and the hydride transfer enzyme diaphorase is capable of reducing the dyes to the colorless leuko form.(ABSTRACT TRUNCATED AT 400 WORDS)

L9 ANSWER 5 OF 16 MEDLINE DUPLICATE 8
AN 88158299 MEDLINE
DN 88158299
TI Novel red absorbing benzo[a]phenoxazinium and benzo[a]phenothiazinium photosensitizers: in vitro evaluation.
AU **Cincotta L**; Foley J W; **Cincotta A H**
SO PHOTOCHEMISTRY AND PHOTOBIOLOGY, (1987 Nov) 46 (5) 751-8.
Journal code: P69. ISSN: 0031-8655.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English

EM 198806

L9 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
AN 1997:740112 HCAPLUS
DN 128:11512
TI Growth inhibition and eradication of tumors using neuroendocrine resetting
therapy and photodynamic therapy
IN **Cincotta, Anthony H.; Cincotta, Louis**
PA Ergo Science Incorporated, USA; General Hospital Corporation; Rowland Institute for Science
SO PCT Int. Appl., 43 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9740829	A1	19971106	WO 1997-US7577	19970415
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
EP 910365	A1	19990428	EP 1997-922668	19970415
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRAI US 1996-16619 19960501
WO 1997-US7577 19970415
AB A method of ablating the growth of or eradicating tumors in mammals having
prolactin, growth hormone, and melatonin daily rhythms involves adjusting one or more of the **prolactin**, growth hormone, and melatonin profiles of the mammal to conform to or approach the corresponding normal profile for healthy members of the same species and sex as said mammal, contacting the cells of the tumor with a photoactive photosensitizer, and, exposing the photosensitizer-contact tumor cells to light of a predetd. wavelength, power d., and energy level.

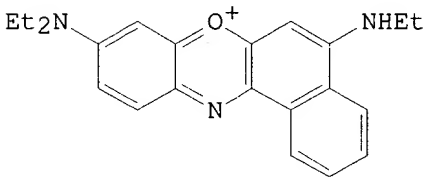
L9 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2000 ACS DUPLICATE 3
AN 1997:525828 HCAPLUS
DN 127:158528
TI Benzophenothiazine and benzoporphyrin dye combination for photodynamic therapy of tumors
IN **Cincotta, Anthony H.; Cincotta, Louis**; Hasan, Tayyaba
PA General Hospital Corp., USA; Rowland Institute for Science
SO PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9726885	A1	19970731	WO 1997-US1436	19970123
W: CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5952329	A	19990914	US 1997-787665	19970123

PRAI US 1996-10485 19960123

AB A method for ablating the growth of or eradicating neoplasms in mammals is provided which involves (a) contacting the cells of the neoplasm with an effective amt. of a combination of photoactive chromophores, and (b) exposing the chromophore-contacted neoplastic cells to light with a wavelength or wavelengths predetd. to be absorbed by the chromophores, the light also having a predetd. power d. and energy level. The photochemotherapeutic effects of a combination of 5-ethylamino-9-diethylaminobenzo[a]phenothiazinium chloride and benzoporphyrin deriv. monoacid A (BPD-MA) in the EMT-6 tumor cell line are shown.

L9 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2000 ACS
AN 1991:602119 HCAPLUS
DN 115:202119
TI Evaluation of Nile Blue E chalcogen analogs as PDT agents
AU Foley, James W.; **Cincotta, Louis; Cincotta, Anthony H.**
CS Rowland Inst. Sci., Cambridge, MA, USA
SO Proc. SPIE-Int. Soc. Opt. Eng. (1991), 1426(Proc. Opt. Methods Tumor Treat. Early Diagn.: Mech. Tech., 1991), 208-15
CODEN: PSISDG; ISSN: 0277-786X
DT Journal
LA English
GI



I

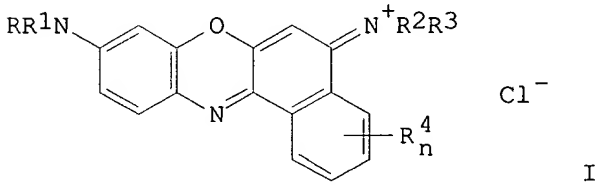
AB The photodynamic therapeutic (PDT) properties of the O-contg. benzophenoxazine dye Nile Blue E (NBEO), (I.HCl), and its S and Se analogs, NBES and NBESe, were evaluated in cell culture using a murine mammary sarcoma (EMT-6) cell line. The photosensitizing efficacies of the dyes correlated with their ability to generate singlet O and to increase in the order NBEO < NBES << NBESe. Under conditions where NBESe kills 97% of the EMT-6 cells, NBES kills only 5% of the cells and NBEO is photoinactive. In the dark, the cytotoxicity of all 3 dyes was minimal. The photoactive benzophenoxazine analogs NBES and NBESe are effective photodynamic agents.

L9 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2000 ACS
AN 1991:117804 HCAPLUS
DN 114:117804
TI Novel benzophenothiazinium photosensitizers: preliminary in vivo results
AU **Cincotta, Anthony H.; Cincotta, Louis;** Foley, James W.
CS Wellman Lab. Photomed., Harvard Med. SCh., Boston, MA, 02114, USA

SO Proc. SPIE-Int. Soc. Opt. Eng. (1990), 1203(Proc. Photodyn. Ther.: Mech. 2, 1990), 202-10
CODEN: PSISDG; ISSN: 0277-786X
DT Journal
LA English
AB The photochemotherapeutic properties of several novel benzophenothiazines were evaluated in vivo in 3 distinct tumor types consisting of a murine sarcoma, human carcinoma, and a rat glioma. S.c. or i.v. administration of dyes to tumor-bearing animals coupled with irradn. of the tumor area with 640 nm light resulted in substantial tumor necrosis 24 h post-photodynamic therapy as detd. by histol. evaluation. Significantly, there was minimal concurrent damage to the surrounding normal tissue. These results offer further evidence for the potential usefulness of benzophenothiazines in the photodynamic therapy of neoplasms.

L9 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2000 ACS
AN 1989:511720 HCAPLUS
DN 111:111720
TI Novel phenothiazinium photosensitizers for photodynamic therapy
AU **Cincotta, Louis;** Foley, James W.; **Cincotta, Anthony H.**
CS Rowland Inst. Sci., Cambridge, MA, 02142, USA
SO Proc. SPIE-Int. Soc. Opt. Eng. (1989), 997(Adv. Photochemother.), 145-53
CODEN: PSISDG; ISSN: 0277-786X
DT Journal; General Review
LA English
AB Phys. and photochem. data on phenothiazine photosensitizers are presented and in vitro photosensitized cell survival of EMT-6 murine mammary cells are examd. following light (6 mW/cm2; 590-700 nm) and phenothiazine exposure. Use of the sensitizers in photodynamic therapy of human neoplasms is briefly discussed.

L9 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2000 ACS
AN 1988:218322 HCAPLUS
DN 108:218322
TI Structure and properties of novel benzo[a]phenoxazinium photochemotherapeutic agents
AU Foley, James W.; **Cincotta, Louis; Cincotta, Anthony H.**
CS Rowland Inst. Sci., Cambridge, MA, 02142, USA
SO Proc. SPIE-Int. Soc. Opt. Eng. (1988), 847(New Dir. Photodyn. Ther.), 90-5
CODEN: PSISDG; ISSN: 0277-786X
DT Journal
LA English
GI



I

AB The structure, properties, tumor localization in vivo in C3H mice, and

photosensitizing efficacy in various carcinoma cell lines in culture with broadband (495-700 and 590-700 nm at 15 and 10 J/cm2, resp.) radiation were studied of several benzophenoxazinium dyes (I where R = H, Et, R1 = H, Et, R2 = H, Me, Et, R3 = H, Et, Me, benzyl, R4 = halo, H, n = 1-2). Photosensitized singlet O formation was used as a parameter of photoactivity. The results in cell culture indicate that several of the dyes have marked photosensitizing activity.

L9 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS DUPLICATE 7
AN 1991:263460 BIOSIS
DN BR40:126340
TI PHOTODYNAMIC THROMBOSIS OF CHOROIDAL VESSELS IN ALBINO RABBITS USING A BENZOPHENOXAZINIUM DYE.
AU GIOVINAZZO V J; SOBEL R S; PATALANO V J II; **CINCOTTA L**; FOLEY J; **CINCOTTA A H**
CS MANHATTAN EYE EAR AND THROAT HOSP., LU ESTHER T. MERTZ RETINAL RES. CENT., NEW YORK, N.Y.
SO ANNUAL SPRING MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY, SARASOTA, FLORIDA, USA, APRIL 28-MAY 3, 1991. INVEST OPHTHALMOL VISUAL SCI. (1991) 32 (4), 1232.
CODEN: IOVSDA. ISSN: 0146-0404.
DT Conference
FS BR; OLD
LA English

L9 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
AN 2000:10563 BIOSIS
DN PREV200000010563
TI Benzophenothiazine and benzoporphyrin dye combination photodynamic therapy of tumors.
AU **Cincotta, Anthony H. (1)**; **Cincotta, Louis**; Hasan, Tayyaba
CS (1) Neuroscience Center, Massachusetts General Hospital, Charlestown, MA USA
ASSIGNEE: Rowland Institute for Science
PI US 5952329 Sep. 14, 1999
SO Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 14, 1999) Vol. 1226, No. 2, pp. No pagination.
ISSN: 0098-1133.
DT Patent
LA English

L9 ANSWER 14 OF 16 BIOSIS COPYRIGHT 2000 BIOSIS
AN 1995:331546 BIOSIS
DN PREV199598345846
TI Combination phototherapy using a benzoporphyrin derivative (BPD-MA) and a benzophenothiazine (ETNBS.
AU **Cincotta, L. (1)**; Foley, J. W.; Szeto, D.; Lampros, E.; **Cincotta, A. H.**
CS (1) Rowland Inst. Sci., Cambridge, MA 02142 USA
SO Photochemistry and Photobiology, (1995) Vol. 61, No. 5 SUPPL., pp. 67S.
Meeting Info.: 23rd Annual Meeting of the American Society for Photobiology Washington, D.C., USA June 17-22, 1995
ISSN: 0031-8655.

DT Conference
LA English

L9 ANSWER 15 OF 16 CONFSCI COPYRIGHT 2000 CSA
AN 2000:3706 CONFSCI
DN 00-003706
TI Properly timed daily administration of **prolactin** enhances anti-tumor responses to photodynamic therapy
AU **Cincotta, A.H.**; Cincotta, E.; **Cincotta, L.**
CS Ergo Sci. Corp., Charlestown, MA, USA
SO Marcel Dekker, Inc., 270 Madison Avenue, New York, NY 10016, USA; fax: 212-685-4540; email: www.dekker.com; URL: intellprop@dekker.com, Abstracts available. Contact Marcel Dekker for price..
Meeting Info.: 993 5027: Joint Meeting of 8th International Conference of Chronopharmacology and Chronotherapeutics and the American Association for Medical Chronobiology and Chronotherapeutics (9935027). Williamsburg, VA (USA). 24-28 Aug 1999. Rothschild Fdtn, Ambulatory Monitoring, Bayer, Elan, Ergo Science, Finkelstein, HealthPartners, Hoechst Marion Roussel, Marcel Dekker, McGovern Fund, Muro, Purdue Pharma, Rhone-Poulenc Rorer, Searle, Sepracor, Space Labs Medical, Univ TX - Houston.
DT Conference
FS DCCP
LA English

L9 ANSWER 16 OF 16 CONFSCI COPYRIGHT 2000 CSA
AN 88:63368 CONFSCI
DN 89036692
TI Novel phenothiazinium photosensitizers for photodynamic therapy
AU **Cincotta, L.**.; **Cincotta, A.**; Foley, J.W.
CS Rowland Inst. Sci.
SO SPIE, P.O. Box 10, Bellingham, WA 98227-0010 (USA). Telephone: 206 676 3290. Telex: 46 7053, Paper No. 997-07.
Meeting Info.: 883 0642: SPIE's International Symposium & Exhibition on Fiber, Optics, Optoelectronics and Laser Applications in Science and Engineering (8830642). Boston, MA (USA). 6-10 Sep 1988. International Society for Optical Engineering (SPIE).
DT Conference
FS DCCP
LA UNAVAILABLE